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The American Heart Journal

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Original Communications

THE VENTRICULAR RATE IN AURICULAR FIBRILLATION STUDIES WITH THE CARDIOTACHOMETER*

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AURICULAR fibrillation is characterized clinically by a rapid, completely irregular, ventricular rate. The accepted explanation of this irregular tachycardia is that the auriculoventricular node and the bundle of His, owing to their refractory period, are unable to transmit the impulses of all the many fibrillary contractions of the auricles which are taking place at a rate of about 450 a minute. In the untreated patient from 100 to 200 auricular impulses a minute reach the ventricles effectively at irregular intervals and initiate ventricular contractions. When a patient with auricular fibrillation is treated with digitalis, a block in the conducting tissue that joins auricles and ventricles is produced which prevents the passage of most of the auricular impulses. In practical therapeutics the ventricular rate is thus reduced to 70 or 80. Excessive doses of digitalis may, however, lead to complete heart-block and idioventricular rhythms of from 30 to 40.

The action of digitalis is twofold: it increases the activity of the vagus inhibitory center, and it acts directly on the conducting tissue, in both ways causing diminished conduction or block. Other methods of stimulating the vagus in patients with auricular fibrillation, such as the administration of physostigmine[1] or pressure on the vagus in the neck or pressure on the eyeball, may also result in a slowing of the ventricular rate. Indeed, Sir Thomas Lewis has said: "If we examine all the known ways of reducing the ventricular rate while the auricles fibrillate, we find that heart-block may always be ascribed as the cause. The same cause alone reduces the ventricular rate in clinical cases."[2]

It would seem on superficial reflection that the ventricular rate of a patient with auricular fibrillation who had been thoroughly digitalized and in whom, therefore, a digitalis block had been produced would be fairly constant, that it would not markedly accelerate or

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retard in response to various extraneous stimuli. But as a matter of fact the ventricular rate of many patients with auricular fibrillation is variable from moment to moment, and this is the subject of the present study.

The rate and rhythm of the normal heart are determined by the sino-auricular node, the well-known pacemaker of the heart, which in turn is governed by the activity of the accelerator and the vagus nerves. When the auricles fibrillate, the sinus node no longer functions, and its chronotropic regulation by the extrinsic nerves of the heart is no longer possible. These nerves now affect the ventricular rate by altering the degree of block in the conducting tissue between auricle and ventricle, and this they do in a degree far greater than is generally recognized. Indeed, so well-informed a man as de Boer[3] has stated that when the auricles fibrillate the nervous regulation of the heart by the vagus and accelerantes is lost for the most part.

Mackenzie[4] recognized the great variability and lability of ventricular rate in patients with auricular fibrillation and believed that this was due to loss of control by the cardiac nerves. He described the great increase in ventricular rate following exercise and noted that after adequate digitalis dosage this reaction could be greatly diminished. He also described patients who at first need digitalis to maintain a slow ventricular rate, but who after a time do very well without digitalis. In these cases he believed the auriculoventricular node had become less excitable.

That vagus stimulation slows the ventricles during auricular fibrillation was demonstrated in animals as early as 1905[5] and many times subsequently, as well as that cutting the vagi of dogs with auricular fibrillation increases the ventricular rate.[6] That the vagus controls the ventricular rate in patients with auricular fibrillation has been shown by Robinson,[7] and by Fahrenkamp,[8] Weil[9] and Semerau[10] who found definite slowing following pressure on the vagus in the neck in 79 per cent of cases of auricular fibrillation. They claim that patients with heart failure and rapid ventricular rates react more often than those who are compensated and whose ventricular rate is slow. There seems to be a parallelism between reactivity to vagus pressure and to digitalis. It is said that hearts which slow under vagus pressure, slow more readily under digitalis medication than do those that do not show the vagus effect.

Kilgore[11] reported cases of auricular fibrillation with a periodic acceleration and retardation of ventricular rate apparently synchronous with the respiratory movements. He attributed the effect to fluctuations of conductivity of the bundle of His determined by the vagus.

Although many have noted an increased ventricular rate after exercise in patients with auricular fibrillation, the most careful study has been made by Blumgart.[12] He found that as compared to the normal

heart the heart with fibrillating auricles responds to exercise by a disproportionate rise in ventricular rate and by a delayed return to the previous resting rate. The same patients were retested after the heart's mechanism had been returned to normal by the administration of quinidine, and a similar reaction was observed. He concludes, therefore, that this exaggerated reaction is due not to the auricular fibrillation but to an additional factor. This factor may well be a valvular lesion or myocardial weakness. I have observed similar reactions in patients with mitral stenosis and regular rhythm. Blumgart found that tincture of digitalis in doses of 30 minims a day did not protect the ventricles from this exaggerated response to exercise. The resting heart rates of his digitalized patients were 76 or over except in two instances in which the rates were 58 and 68. Even in these cases he observed rises of ventricular rate of 67 and 62 respectively after exercise. Mackenzie[13] on the other hand claims that if adequate doses of digitalis are given this exaggerated response of the ventricles to effort can be controlled. Lundsgaard[14] has made similar observations.

Gallavardin[15] has described patients with auricular fibrillation with ventricular rates of from 35 to 50 due to partial heart-block and attacks of syncope, who showed an increase in ventricular rate (in one case from 40 to 117) following exercise.

The acceleration of ventricular rate in patients with auricular fibrillation following the administration of atropine has long been known.[16]

In auricular flutter the ventricles react as a rule to every second, third or fourth auricular beat. Vagus stimulation or digitalis slows the ventricles by producing a partial heart-block, exercise and excitement exert the reverse effect.[17]

It is evident from these many observations that even when the auricles fibrillate or flutter the ventricular rate is under control of the extrinsic nerves of the heart. The significance of this in the clinic, however, is not fully appreciated.

I have studied the ventricular rate in a group of patients with auricular fibrillation and auricular flutter by means of my cardiotachometer.[18] This is an instrument which counts the ventricular rate automatically over long periods of time while the subject is pursuing his ordinary physical activities. Registration is not disturbed by exercise. The action current of the heart is led from the chest by special electrodes through wires from 60 to 100 feet long to a specially constructed radio amplifier which amplifies it some 6000 times. The amplified current operates a relay system which in turn operates an electromagnetic counter which counts the heartbeats. In addition a pen writing on a moving tape records every beat of the heart. Patients were kept under observation from fourteen to twenty-four hours.

Figs. 1 and 2 represent twenty-four-hour records of the ventricular rate in a girl fourteen years old with mitral stenosis and auricular fibrillation; Fig. 1 undigitalized, Fig. 2 after 23 c.c. of tincture of digitalis had been administered in the preceding ten days. The patient was in bed unless it is otherwise noted. The great lability of the heart rate is apparent in both records. The range of variability is if any-

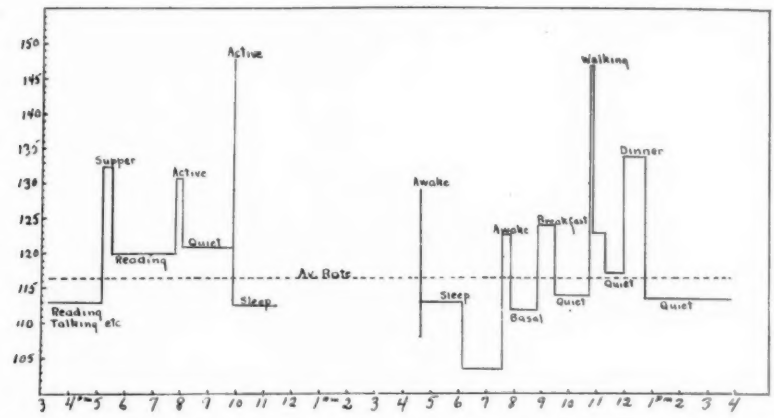

Fig. 1.—Auricular fibrillation; undigitalized. Total time 19 hours, 36 minutes. Total heartbeats 137,101.

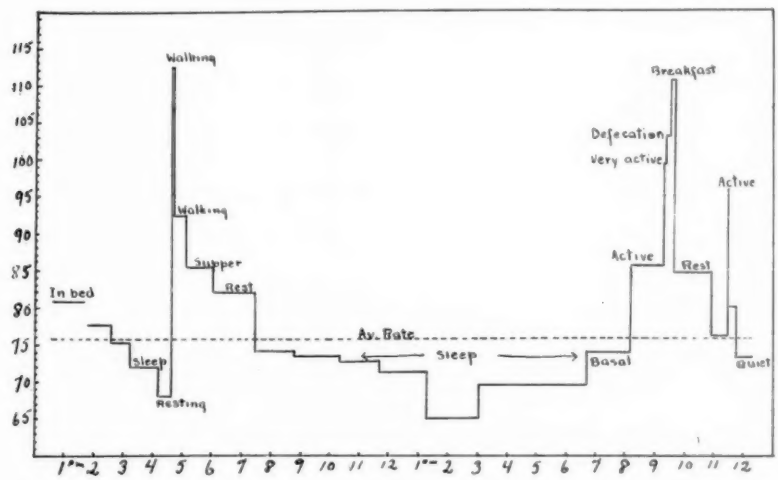

Fig. 2.—Auricular fibrillation; digitalized. Total time 23 hours, 33 minutes. Total heartbeats 107,291.

thing greater when the patient is under the influence of digitalis but takes place at a lower level. It is striking to see how relatively slight activity, such as that involved in eating, will accelerate the ventricles from 15 to 20 beats. Walking provokes an increase in rate of from 33 to 46 beats a minute. Sleep on the other hand slows the ventricular rate, the drop being most marked after several hours of sleep. Fig. 3,

representing very frequent readings in a man with auricular fibrillation who was under the influence of digitalis, shows these constant variations in ventricular rate still more clearly. A simple conversation suffices to produce an acceleration of 18 beats; walking provokes a rise of 73 beats; eating provokes a rise of 8 beats a minute; and a short nap reduces the rate by 16 beats a minute.

These charts demonstrate very clearly that if the generally accepted explanation of the mechanism of ventricular activity in auricular fibrillation is correct—and there is every reason to suppose that it is—the frequency of ventricular contraction is under control of the vagus and accelerator nerves. The activity of these nerves is con-

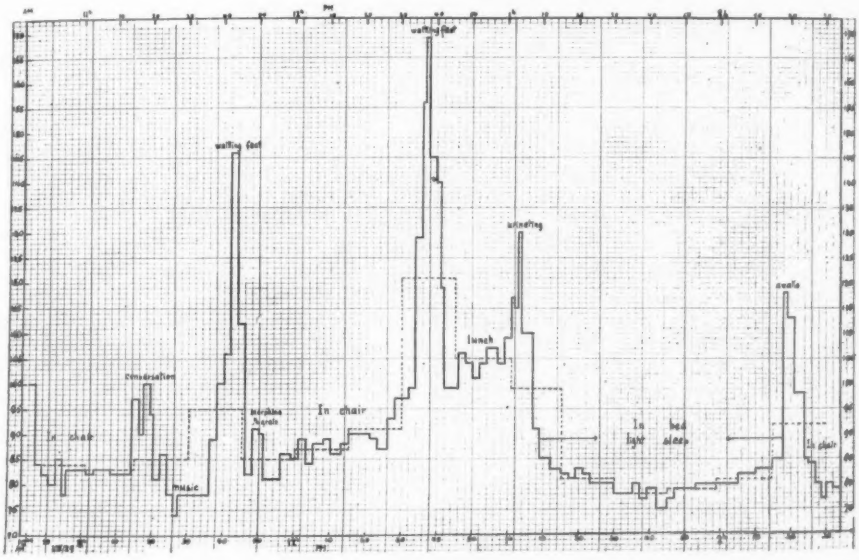

Fig. 3.—Auricular fibrillation. Variability in rate. ——— readings every few minutes; - - - - readings every 15 minutes.

stantly manifest by changes in rate in response to manifold stimuli, just as in normal sinus rhythm. Their mode of action in auricular fibrillation is different, however, for instead of regulating the speed of impulse formation in the sino-auricular node, they act by altering the refractory period or the conductivity of the auriculoventricular node and the bundle of His. In view of the fact that both vagus and sympathetic inosculate around the auriculoventricular node, as well as around the sinus node, this phenomenon is quite comprehensible.

Individuals with normal sinus rhythm show widely varying degrees of lability of heart rate. In those who are phlegmatic the rate tends to be stable; in those who are high-strung, acceleration and retardation of the heart in response to the manifold stimuli of everyday life are excessive. A similar increased lability is seen in patients with

Graves' disease and during fevers as well as during convalescence from acute infectious diseases. Patients with auricular fibrillation vary similarly in the degree of lability of their ventricular rates. These different types of ventricular response depend not on the auricular fibrillation as such but on the activity of the extrinsic cardiac nerves. Their recognition is of the utmost importance in therapeutics, for successful treatment with digitalis predicates an understanding of the effect of neurogenic factors on ventricular rate.

Patients with auricular fibrillation have been grouped according to their ventricular rates. Semerau[9] in a study of 111 cases found 71 cases or 64 per cent with rapid rates, i.e., rates over 80, and 37 cases or 33 per cent with slow rates, i.e., under 80. About 10 per cent of the cases had ventricular rates under 60. This distinction was made by Mackenzie[19] in 1911, who noted that slow rates were found in older patients suffering from the degenerative forms of heart disease. In these patients, in his experience, the ventricles slowed but little under digitalis therapy. He attributed the infrequent ventricular beats to organic block in the conducting tissue. Later authors have largely followed his interpretation.[20]

But this explanation is not altogether satisfactory. Block in the auriculoventricular conducting tissue may be due to actual lesions involving the tract; it may be functional due to an increase in the number of auricular impulses showered upon it; it may be due to impaired nutrition; it may be determined by vagus action or by the effect of drugs, such as digitalis. On the other hand it has been shown experimentally that conduction may be improved by stimulation of the accelerator nerves and that in auricular fibrillation this leads to an increased number of ventricular beats.[21] Both Gerhardt[22] and Cushny[23] saw in this mechanism the explanation of the phenomenon that in patients with auricular fibrillation and a slow ventricular rate the rate becomes rapid when the heart becomes insufficient due to overexertion or infection. Exercise hastens the ventricular rate in the same way. This is quite analogous to the reaction to exercise noted in certain patients with complete heart-block in whom the block is temporarily lifted, due to the "work reflex" via the accelerans.[24]

It is evident that the varying ventricular rates encountered in patients with auricular fibrillation cannot for the most part be explained by assuming different degrees of heart-block on an anatomical basis. It seems clear from the evidence in the literature as well as from the lability of rate shown in my records that the activity of the extrinsic nerves of the heart must play a considerable rôle. Hoffman[25] is one of the few authors to emphasize this view. Robinson[20] points out that the cause of ventricular slowing following rest is unknown.

Indeed a number of facts demand explanation. Why is the ventricular rate usually very rapid at the first onset of auricular fibrilla-

tion, particularly when the fibrillation occurs in paroxysms; and why does the ventricular rate become slower when the disturbance of the auricular mechanism becomes permanently established? Why do certain of these patients at first exhibit rapid ventricular rates requiring continuous digitalis dosage and then after a period of such medication show ventricular rates below 80 long after digitalis has been discontinued? Why do these same patients after an intercurrent infection or physical overstrain revert to high ventricular rates and again require large amounts of digitalis? Why is the ventricular rate of patients with exophthalmic goiter and auricular fibrillation rapid, as a rule, even after digitalis medication? I have observed this a number

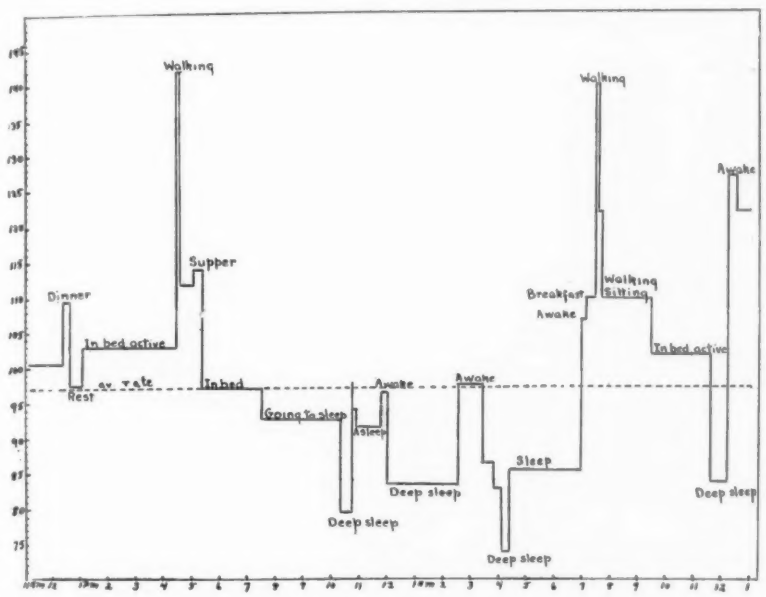

Fig. 4.—Auricular fibrillation; partly digitalized. Total time 25 hours, 49 minutes. Total heartbeats 150,304.

of times, and it is well shown in the case reports of Baumgartner, Webb, and Schoonmaker,[26] although they do not draw attention to it.

I believe that these phenomena can be explained on the basis of alteration of tone of the vagus and accelerator nerves. For instance, the sympathetic nervous system is hyperactive in exophthalmic goiter. This would increase the conductivity of the conducting tissue of the heart and so allow a more rapid ventricular rate. There is further evidence of the correctness of this view.

Patients with auricular fibrillation may be classed in two groups: those with a labile and those with a relatively stable ventricular rate. Individuals with labile ventricular rates are usually high-strung and nervous; they correspond to individuals with normal rhythm and

symptoms of neurocirculatory asthenia. Emotional surges and physical exertion provoke exaggerated rises in ventricular rate; rest and sleep are accompanied by low ventricular rates. This lability of ventricular response persists after thorough digitalization. Individuals with stable ventricular rates are, as a rule, calm and phlegmatic. The ventricular rate responds only to a moderate degree to emotion and exercise and is readily kept under control by digitalis.

Case 1, a young man with rheumatic mitral stenosis and aortic insufficiency, had a ventricular rate of about 200 when first seen. Pressure on the eyeball effected marked slowing of the ventricles and made possible the recognition of the absolute irregularity which was ob-

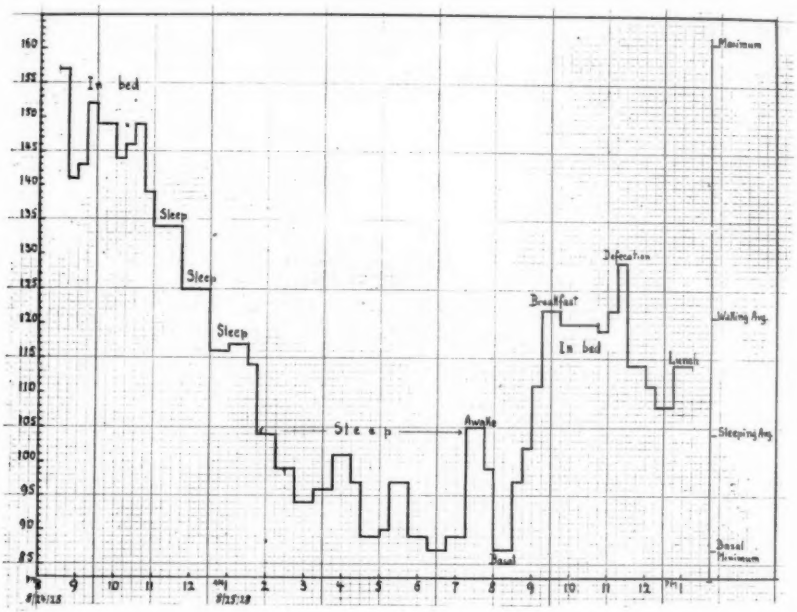

Fig. 5.—Auricular fibrillation; 75 c.c. tincture of digitalis, July 22-August 17, none since then. Total time 16 hours, 53 minutes. Total heartbeats 114,251.

secured by the rapid heart action. The patient was nervous and high-strung and had a marked anxiety neurosis. Although he received 3 c.c. of tincture of digitalis daily for several weeks, his ventricular rate remained rapid and very labile. His cardiotachometric record (Fig. 4) was taken after he had received 28 c.c. of tincture of digitalis in thirteen days following the previous dosage. The lability of ventricular rate, the exaggerated response to exercise, the marked drop during sleep are evident.

Cases 2 and 3 are similar in type: high-strung individuals whose ventricular rates were usually rapid during their waking hours, slowing to 85 and 76 during sleep. Case 2, a man thirty-seven years old, with rheumatic mitral stenosis and cardiac insufficiency, under heavy doses

of digitalis had a ventricular rate of 84, yet at other times in spite of even larger dosage the rate was 120. Several times a week he had paroxysmal attacks of rapid ventricular rate of from 150 to 160 accompanied by pain in the precordium and a sense of choking. The cardiotachometric record (Fig. 5) clearly illustrates the marked lability of ventricular rate and in particular the profound drop during sleep. This reduced ventricular rate during sleep is shown by all patients with auricular fibrillation and is analogous to the drop in rate observed in individuals with normal sinus rhythm. It is due apparently to the great diminution during sleep of physical and psychic stimuli which act reflexly on the heart. Subsequently this patient received much larger doses of digitalis—51 c.c. of the tincture in ten

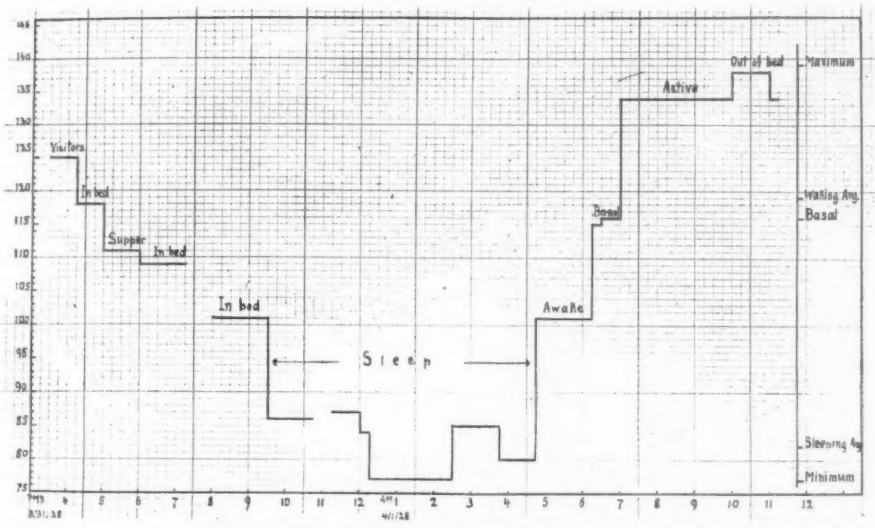

Fig. 6.—Auricular fibrillation, tincture of digitalis 33 c.c. from March 20-March 28. Total time 18 hours, 38 minutes. Total heartbeats 118,148.

days, or three times the body-weight dose. This kept his ventricular rate at about 86 even during his waking hours.

Case 3, a man with rheumatic mitral stenosis, aortic insufficiency, and auricular fibrillation had received 33 c.c. of the tincture of digitalis in eight days. The ventricular rate at rest was 85. The slightest excitement, such as that occasioned by the approach of a physician or a nurse, induced a rate in the neighborhood of 160, which dropped only gradually. He has a marked anxiety neurosis, and many of the symptoms of neurocirculatory asthenia. The periods of rapid ventricular rate are accompanied by flushing of the face. His curve (Fig. 6) shows the rapidity of his ventricles during the day and the marked drop during sleep.

Cases 4 and 5 show the contrast between the labile and the phlegmatic types to better advantage. They are two boys with rheumatic

valvular disease and auricular fibrillation, both thirteen years old. The first has mitral stenosis, and the second has mitral stenosis and aortic insufficiency.

In Case 4 (Fig. 7) without digitalis the ventricular rate ranged from 81 to 120 and was fairly steady. After small doses of digitalis, only 13 c.c. of the tincture spread over twenty-one days, the rate dropped considerably and became still more stable. On the other hand Case 5 (Fig. 8) when untreated had a ventricular rate which ranged from 98 to 167 and did not drop below 100 during sleep. After 24 c.c. of tincture of digitalis in seven days his ventricular rate showed a very satisfactory drop but not so low a range as that of the other boy.

It must be borne in mind that all these patients have hearts with other damage in addition to the auricular fibrillation. They have valvular disease and varying degrees of myocardial insufficiency. Such hearts even with normal rhythms show a marked lability of rate in

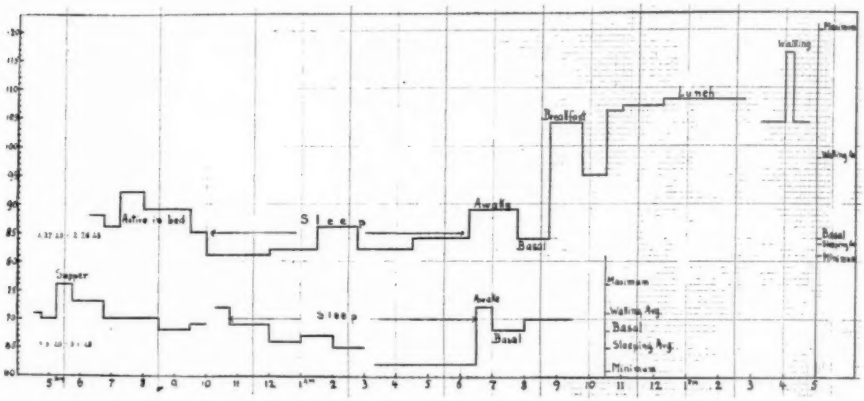

Fig. 7-*a*.—Auricular fibrillation; undigitalized. Total time 22 hours, 1 minute. Total heartbeats 121,362.

b.—Auricular fibrillation; digitalized. Tincture digitalis 10 c.c. from May 10-May 20. Tincture of digitalis 3 c.c. from May 26-May 31. Total time 16 hours, 22 minutes. Total heartbeats 66,670.

response to various stimuli. That this plays a rôle in the cases under discussion has been shown by Blumgart.[12] But even this effect must take place through the intermediation of the nervous system. Although the ventricles of hearts with fibrillating auricles are under control of the cardiac nerves and react by changes in rate to the many stimuli engendered by the bodily functions, this regulation is not so well adapted to fit the cardiac response to the circulatory needs of the body. There is overshooting; the reaction is often excessive.

All of the above observations lead to a number of interesting and practical conclusions. They illustrate again very clearly that the action of a drug depends just as much on the reaction of the individual subject as on the innate properties of the drug. The dosage of digitalis necessary to achieve a certain effect will depend as much upon

the vagus-accelerator tone as upon the body weight of the patient. Patients with different nervous constitutions react differently to identical doses of digitalis when their auricles are fibrillating. Those who are high-strung and anxious have rapid ventricular rates, and larger quantities of digitalis are required to slow the ventricles. The ventricular rate remains labile even after much digitalis has been administered and after the characteristic changes in the T-wave, indicative of digitalis action, have appeared. Individuals who are more phlegmatic tend to have slower ventricular rates which are readily retarded and stabilized by the usual doses of digitalis. The first group

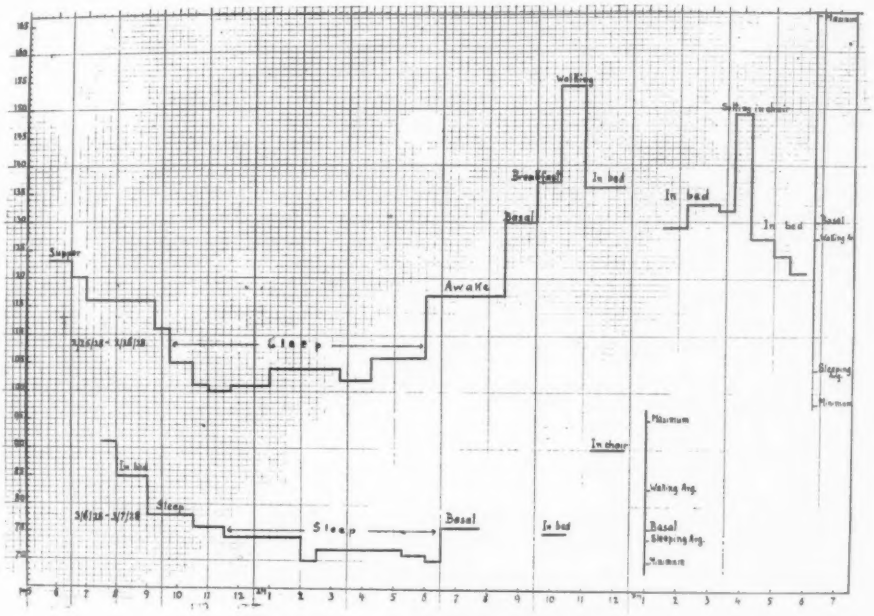

Fig. 8-*a*.—Auricular fibrillation; undigitalized. Total time 23 hours, 3 minutes. Total heartbeats 163,913.

b.—Auricular fibrillation; digitalized. Tincture of digitalis 24 c.c. from March 1-March 7. Total time 13 hours, 28 minutes. Total heartbeats 61,831.

seems to tolerate very large doses of digitalis without exhibiting any toxic action such as nausea or bigeminy.

Making due allowance for different rates of absorption and elimination in different individuals, this varying tolerance to the drug seems to be analogous to the well-known variation in tolerance of different persons to atropine. Patients with spastic colitis, for instance, tolerate infinitely larger doses of atropine than do other individuals. In the case of digitalis, those in whom there is apparent overactivity of the sympathetic nervous system are resistant to the action of the drug.

It would seem advisable in the labile group of patients with auricular fibrillation to supplement the action of digitalis with sedatives and

psychotherapy. It is also important to remember that these patients require larger quantities of digitalis than their body-weight calculation would indicate. The great value of rest and sleep as restoratives in cardiac insufficiency is evident from the graphs.

SUMMARY

The ventricular rate of patients with auricular fibrillation has been studied by means of the cardiotachometer. It has been shown that the ventricular rate is variable, that it accelerates in response to the slightest exertion or emotion, and that it slows during rest and particularly during sleep. All the evidence indicates that the ventricular rate in these patients is under control of the cardiac nerves and that alterations in rate are governed by neurogenically determined changes in conductivity of the specific conducting tissue of the heart. The changes in ventricular rate arise, apparently, in response to the varying physiological needs of the body just as in health, but the reaction is not so well regulated and is often excessive.

Patients with auricular fibrillation may be classed in two groups: those with labile and those with stable ventricular rates. The former are high-strung and nervous and correspond to patients with neurocirculatory asthenia. Their ventricular rates tend to be rapid, and quantities of digitalis in excess of the body-weight dose are required to keep the ventricular action slow and stable. In addition it would seem that sedative and psychotherapeutic treatment should assist materially in slowing the ventricles. In the stable group the ventricles do not exhibit such an exaggerated response to physical and emotional stimuli and can readily be kept under control by the usual methods of digitalis therapy.

The value of rest and sleep in the treatment of patients with auricular fibrillation, a fact well known, is forcefully demonstrated by actual count of the number of heartbeats by means of the cardiotachometer.

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THE ORAL ADMINISTRATION OF CALCIUM CHLORIDE IN CONGESTIVE HEART FAILURE*

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IN THE treatment of patients suffering from heart failure there are often present edema and collections of fluid in the serous cavities which are refractory to removal by drugs, such as digitalis, novasurol, and the theobromine diuretics which are commonly in use. For this reason it is desirable to test thoroughly measures which promise to be of benefit in these cases.

In 1921 and 1922 Blum[1] and his coworkers described a new group of diuretics. According to their conception edema is caused by the retention of sodium ions; sodium ions in being retained hold water which accumulates in the tissues and serous cavities. They found that diuresis was induced in cases of edema of nephritic origin, in cirrhosis of the liver with ascites and in inflammation of the liver with fluid accumulations by the oral administration of salts of calcium, potassium and strontium. They thought that the sodium ions in the tissues were replaced by calcium, potassium or strontium ions; that they were excreted as sodium chloride and in being excreted carried water with them. In this way water was removed from the tissues. They were of the opinion that diuresis occurred by the "replacement of ions." Though they believed that this group of diuretics was effective in the conditions just mentioned, they stated that they were usually ineffective in edema due to heart failure and gave warning that the use of them in these cases was dangerous.

At the time this series of papers appeared we had under observation a patient whom we were unable to free of edema by limitation of fluids, by the use of a diet free of salt or by the administration of digitalis and the usual diuretics. This patient we succeeded in making free of edema by giving calcium chloride by mouth. From this experience we were led to give the salt to a small number of patients; a preliminary report has already appeared.[2]

Since the appearance of Blum's papers, Keith, Barrier and Whelan[3] have reported the occurrence of satisfactory diuresis in cases in which there was edema due to nephritis, following the report of Atchley, Loeb and Benedict[4] concerning a patient who suffered from edema occurring in the course of diabetes. Recently, Segall and White,[5] after giving calcium chloride to a number of patients, concluded that it

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may be employed as a diuretic "in cases of cardiac failure with edema in which constant rest in bed, digitalization and administration of various diuretics have not resulted in satisfactory diuresis."

METHOD OF INVESTIGATION

Calcium chloride was administered orally to six patients suffering from heart failure in whom edema was present. All patients were subjected to a preliminary period of rest in bed. They were given a fixed amount of fluid per day. These conditions were maintained during the administration of calcium chloride. It was given as a concentrated solution. Divided into two doses, 15 gm. were usually given a day. It was followed by a small amount of orange juice for relief of the bitter taste. After taking calcium chloride patients complained occasionally of a burning sensation in the epigastrium or of abdominal cramps. These symptoms were, however, not severe. One patient (Case 3) vomited on one occasion and another (Case 2) on two occasions. Other untoward symptoms were not encountered. In some observations calcium chloride was given alone; in others it was given to patients who had first received a sufficient amount of digitalis to affect the T-wave of the electrocardiogram or to slow the ventricular rate in auricular fibrillation. In still further observations, the administration of calcium chloride was followed by that of digitalis. A few patients were the subjects of the three sets of observations. Most of the patients were those to whom other diuretics had been given without effect.

OBSERVATIONS

CASE 1.—S. F. (See Case 18, Stewart[6]) was a woman, 24 years old. She was under treatment in the hospital from September 13, 1922, until July 29, 1924. The diagnosis* was: *Etiological:* acute rheumatic fever (inactive); *anatomical:* cardiac hypertrophy, mitral stenosis and insufficiency, aortic insufficiency, left ventricular preponderance; *physiological:* auricular fibrillation, congestive heart failure. She was admitted to hospital because of shortness of breath and edema of the legs. She had suffered from numerous attacks of acute rheumatic fever between the ages of five and eighteen years. Cardiac involvement occurred at the time of the first attack. The heart was very much enlarged. There were signs of mitral stenosis and insufficiency and of aortic insufficiency. The systolic blood pressure measured 110 to 115 mm. of mercury and the diastolic 70 mm. Auricular fibrillation was present. From September, 1922, until June, 1923, the patient was given a diet free of salt, and the fluid-intake was restricted to 1500 c.c. a day. She was given digitalis either alone or combined with diuretin or theocin. By these means sporadic increases in volume of urine were obtained, but only rarely did the increase continue long enough to make the patient free of edema for even a day or two. Finally, the patient was given calcium chloride 15 gm. a day by mouth, on four days. Up to this time the volume of urine had been 1300 c.c. a day when she was taking 1500 c.c. of fluid a day. On the first day that calcium chloride was given the volume of urine was 1265 c.c., 673 c.c. on the second, 1575

*The diagnoses conform to the nomenclature for cardiac diagnosis approved by the American Heart Association. AM. HEART J. 2: 202, 1926-1927.

c.c. on the third, 1970 c.c. on the fourth, and 2210 c.c., 1706 c.c. and 1769 c.c. on the three days following, although during these calcium chloride was not given. The patient lost 0.8 kg. in weight, and the edema disappeared. Edema reappeared as soon as diuresis stopped, and on the third day after the end of diuresis, calcium chloride was accordingly given again on five days. One day only the output rose to 1800 c.c. Edema decreased. After an interval of three days (during which the volume of urine decreased to 400 c.c. per day, and edema increased) calcium chloride was given again. The day the administration of calcium chloride was begun, digitan 0.9 gm. was also given. The output rose to 1730 c.c., 1750 c.c., 1666 c.c., 1325 c.c., 800 c.c., and 1805 c.c. respectively on the six days that it was given and remained 1853 c.c., 1880 c.c., 1438 c.c., and 1790 c.c., on the four days afterward; it fell then to 1200 c.c. The patient lost 1.5 kg. in weight and became free of edema. She was given no drugs from June 27 to July 20. At the end of this time edema recurred and she gained 3.0 kg. in weight; the output of urine

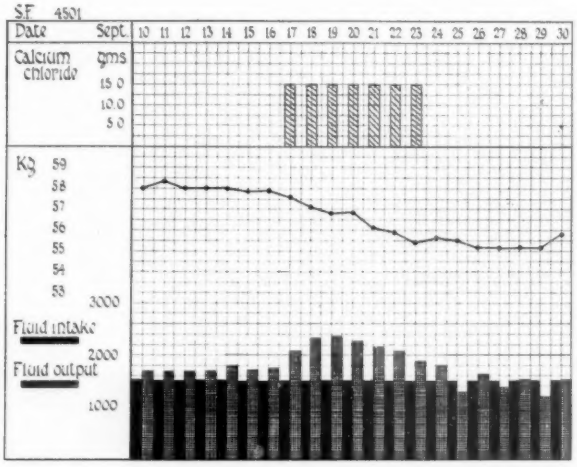

Fig. 1.—Shows the effect of the administration of calcium chloride upon the volume of urine in Case 1.

was approximately 1000 c.c. a day. Calcium chloride was then given on four days. On the first three days the output of urine was 705 c.c., 750 c.c., and 785 c.c., respectively. Diuresis did not begin until the fourth day when the output rose to 1595 c.c., and was 1695 c.c., and 2065 c.c. on the next two days. The patient lost 1 kg. in weight. Edema again decreased, and a few days later when digitan 0.7 gm. was given the output increased for a day or two and she became free of edema. She was given maintenance doses of digitalis. She was allowed to sit up; edema recurred, however, and she remained in bed. Beginning September 17 calcium chloride was given on seven days (Fig. 1). The output had been, on the average, 1700 c.c. a day before calcium chloride was given. During the seven days that calcium chloride was given, the volume of urine rose to 2060 c.c., 2362 c.c., 2178 c.c., 2284 c.c., 2190 c.c., 2085 c.c., and 1865 c.c. respectively; it was 1818 c.c. the next day and then fell to 1291 c.c. During the period of diuresis the patient lost 2.5 kg. in weight, and she became free of edema. She received no drugs from September 23 to November 12. Edema recurred. Calcium chloride was again given during five days. The output rose from 1000 c.c. to 1200 c.c. a day, to 1425 c.c., 1475 c.c., 2043 c.c., 1890 c.c., and 1890 c.c. respectively, and the patient lost 2 kg. At the end of this time there was only a slight trace of edema

of one ankle. The patient was then given digitalis; a slight increase in output of urine occurred. In spite of this, edema persisted and she gained weight. Beginning December 3, calcium chloride was given on five days. The output rose from 1400 c.c. to 1600 c.c., and remained at that amount for seven days.

Summary.—This patient with edema due to heart failure was given calcium chloride by mouth on seven occasions, four times alone and three times combined with full therapeutic doses of digitalis (0.7 gm. to 0.9 gm.). Diuresis followed on each occasion and on four of them she became free of edema. Calcium chloride appeared to be equally effective whether the patient was or was not under the influence of digitalis; the effect which could be ascribed to digitalis did not appear, however, to be greater when this drug was given in combination with

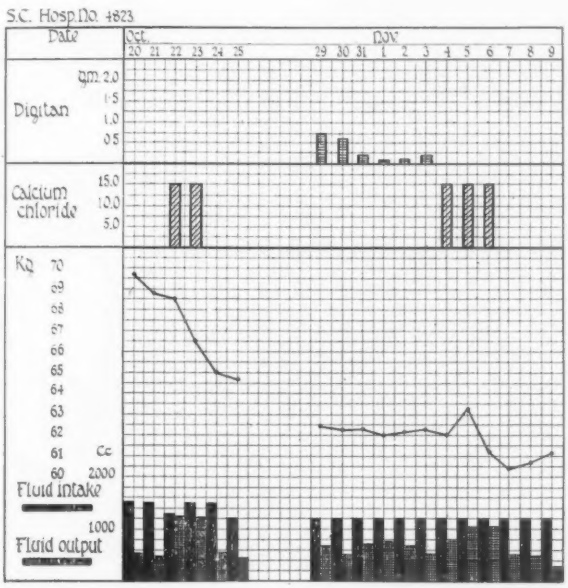

Fig. 2.—Shows the effect of the administration of calcium chloride upon the volume of urine in Case 2, first when given alone, and second when given after the administration of digitalis.

calcium chloride than when given alone, that is to say a synergistic action between these two drugs was not demonstrated in the case of this patient.

Case 2.—S. C. (See Case 14, Stewart[6]). This patient was a man, 66 years old. He was admitted to hospital complaining of shortness of breath of five years duration. The cardiac diagnosis of this patient was: *Etiological:* arteriosclerosis; *anatomical:* cardiac hypertrophy, mitral insufficiency, left ventricular preponderance; *physiological:* auricular fibrillation, congestive heart failure. There was no history of acute rheumatic fever. The heart was enlarged. Auricular fibrillation was present. A soft systolic murmur was heard at the apex. The systolic blood pressure was 150 mm. of mercury and the diastolic 80 mm. Cheyne-Stokes respirations were present. There were moist râles at the bases of the lungs posteriorly.

There was marked edema of the legs. The Wassermann reaction of the blood was negative.

The fluid intake was limited to 1500 c.c. a day. After he had been in bed for three days he was given, on October 22, 1923, calcium chloride 15 gm. (Fig. 2). The output of urine, which had been 497 c.c. the day before rose now to 1210 c.c. The following day, when the same amount of calcium chloride was given it was 1226 c.c.; the edema disappeared. The next day calcium chloride was not given; the output of urine fell to 525 c.c. On October 25 the fluid intake was reduced to 1200 c.c. per day. The volume of urine remained low until October 26 and 27. On each of these days calcium chloride 15 gm. was given and the output rose to 621 c.c. and 1215 c.c. respectively; a decrease then occurred. The patient was given digitalis until the ventricular rate was slow and the electrocardiogram showed changes in the T-wave. There was one day (November 1) a slight increase in output to 770 c.c. He was then given calcium chloride 15 gm. a day on three days. The output amounted to 805 c.c. on the first, 1122 c.c. on the second and 1136 c.c. on the third day, but fell to 590 c.c. the next day when calcium chloride was not given. The patient was without medication for the next eleven days; the output of urine varied between 250 c.c. and 500 c.c. a day. A slight degree of edema recurred. Beginning November 18 he was given calcium chloride again, 15 gm. a day on 4 days. There was a slight but definite increase in output of urine amounting to 835 c.c. a day. During this time he lost weight and edema disappeared. He was then given digitalis from November 23 until December 10. Toward the end of this period the volume of urine was slightly increased, and he lost 2 kg. in weight. One day the volume of urine was 1100 c.c.; it then decreased. On December 12 he was given calcium chloride 15 gm.; the output rose from 770 c.c. to 1224 c.c. The next two days, when given the same amount of calcium chloride, it was 1105 c.c. and 1103 c.c. respectively; on the fourth day when he received calcium chloride 7.5 gm., the output fell to 516 c.c. and remained at that level. During the four days it was given he lost 2 kg. in weight. He was now given a sufficiently large amount of digitalis daily to keep the ventricular rate slow. About six weeks later acute dilatation of the heart occurred, and the patient died. An autopsy was performed. The diagnosis was as follows: General arteriosclerosis; arteriosclerotic involvement of the cusps of the aortic valves; cardiac hypertrophy; aneurysm of the abdominal aorta*; infarcts of the kidneys; arteriosclerosis of the kidneys; terminal broncho-pneumonia; venous stasis of the organs.

Summary.—Calcium chloride was given then on six occasions to this patient, on three without digitalis, on two, following the administration of digitalis, and on one the use of digitalis was followed by calcium chloride. The administration of calcium chloride was always accompanied by increase in volume of urine; it was often more than doubled on the days the drug was given. The resulting diuresis was sufficient to free the patient of edema. It appeared to be effective whether it was given when the patient was or was not under the influence of digitalis. Vomiting occurred twice during its administration.

CASE 3. I. K. This patient was a man 37 years old. He complained of shortness of breath, palpitation and edema. The cardiac diagnosis was: *Etiological:* unknown; *anatomical:* cardiac hypertrophy, mitral stenosis and insufficiency, right ventricular preponderance; *physiological:* auricular fibrillation, congestive heart failure. Cyanosis was present. The heart was enlarged. There were signs of

*The patient frequently complained of abdominal pain. The abdomen presented no abnormality on physical examination.

mitral stenosis and insufficiency. The systolic blood pressure was 115 mm. of mercury and the diastolic 75 mm. There was free fluid in the right pleural cavity. Moist râles were heard in both lungs. The liver was enlarged; ascites was present. There was edema of the lower extremities.

The patient was so ill that digitalis was given at once. The ventricular rate became slow. While taking 1200 c.c. of fluid a day the output of urine remained between 295 c.c. and 519 c.c. per day. On the seventh day after admission to the hospital (the patient was still under the influence of digitalis) he was given calcium chloride 15 gm. The volume of urine on that day was 489 c.c. The following day, when calcium chloride was given again, the output was 618 c.c. On continuing its administration on the third and fourth days the output was 810 c.c. and 655 c.c., respectively. On the fifth day it was not given, and it fell to 524 c.c. Then it gradually decreased to 300 c.c. per day. Later, satisfactory diuresis occurred when novasurol was given.

Summary.—This patient was under the influence of digitalis when calcium chloride was given. There occurred a very slight increase in the output of urine. It was not sufficient, however, to have an effect on the accumulation of fluid in the tissues and serous cavities. Vomiting occurred once during administration of the salt.

CASE 4. G. B., (See Case 17, Stewart[6]). This patient was a man, 69 years old. He complained of shortness of breath and edema. The cardiac diagnosis was: *Etiological:* arteriosclerosis; *anatomical:* cardiac hypertrophy, aortic stenosis and insufficiency, mitral insufficiency, left ventricular preponderance; *physiological:* auricular fibrillation, congestive heart failure. There was no history of acute rheumatic fever. The heart was enlarged; auricular fibrillation was present. Over the base there was a rough systolic and a soft diastolic murmur. Soft systolic and diastolic murmurs were also heard at the apex. The systolic blood pressure was 120 mm. of mercury and the diastolic 90 mm. There was free fluid in the right pleural cavity. The liver was enlarged; ascites was present. There was marked edema of the legs. The Wassermann reaction of the blood was negative.

The patient was given a large amount of digitalis. Diuresis did not occur. The output of urine remained 500 c.c. when he was taking 1000 c.c. of fluid a day. At a time when he was not under the influence of digitalis he was given calcium chloride 15 gm. a day on four days. On these days the output was 680 c.c., 755 c.c., 610 c.c., and 788 c.c., respectively. During this time there was no loss of weight, and the edema did not decrease. Later, after giving diuretin the volume of urine increased to 1588 c.c. on one day. About ten days later the patient died suddenly. An autopsy was performed. The diagnosis was: chronic cardiac valvular disease (aortic); general arteriosclerosis; perforation of the interventricular septum; contraction scar in the conus of the pulmonary artery; hypertrophy and dilatation of the right and the left ventricles; chronic myocarditis; thrombosis of the pulmonary artery; edema, ascites, hydropericardium; hydrothorax, venous congestion of the organs; arteriosclerosis of the kidneys; cysts of the kidneys.

Summary.—Calcium chloride was given to this patient when he was not under the influence of digitalis. The slight increase in output of urine which occurred was not sufficient to influence the degree of congestive heart failure.

CASE 5. A. B. This patient was a female, 44 years old. She complained of swelling of the abdomen, shortness of breath and edema. The diagnosis was: *Etiological:* acute rheumatic fever (inactive); *anatomical:* mitral stenosis and

insufficiency, cardiac hypertrophy, right ventricular preponderance; *physiological:* normal sinus rhythm, congestive heart failure. She suffered from an attack of acute rheumatic fever 7 years before. Involvement of the heart occurred at that time. Fluid had been removed from the abdominal cavity by paracentesis every three weeks during the last 20 months. The heart was enlarged. The rhythm was normal. There were signs of mitral stenosis and insufficiency. The systolic blood pressure was 100 mm. of mercury and the diastolic 80 mm. The lungs were clear. There was marked ascites. The liver was enlarged. There was marked edema.

During the first 5 days in hospital the patient gained 2.5 kg. in weight. The volume of urine was not more than 319 c.c. per day. Calcium chloride 10 gm. a day was given on 5 days. The output on these days was 315 c.c., 333 c.c., 474 c.c., 565 c.c., and 515 c.c., respectively. The next day, when it was not given, the output was 510 c.c. and then fell to 300 c.c. per day. Digitalis and novasurol were given also without diuretic effect. Ascites increased so rapidly that abdominal paracentesis was performed and 13 liters of fluid were removed. The patient died suddenly 4 days later. An autopsy was performed. The diagnosis at autopsy was as follows: chronic cardiac valvular disease (mitral stenosis); ascites; hydropericardium; chronic passive congestion of the liver, spleen and pancreas; chronic peritonitis, perihepatitis, perisplenitis; cirrhosis of the liver.

Summary.—The oral administration of calcium chloride to this patient was followed by an increase of only a few hundred cubic centimeters in the volume of urine. In this instance its use was not combined with the administration of digitalis.

CASE 6. E. A. This patient was a male, 72 years old. He complained of shortness of breath and swelling of the legs. The cardiac diagnosis was: *Etiological:* arteriosclerosis; *anatomical:* cardiac hypertrophy, chronic myocarditis, left ventricular preponderance; *physiological:* normal sinus rhythm, congestive heart failure. The heart was enlarged. The rhythm was regular. The sounds were clear both at the apex and over the base. The systolic blood pressure was 150 mm. of mercury and the diastolic 110 mm. There was fluid in the right pleural cavity. The liver was enlarged. Marked edema of the legs was present. The Wassermann reaction of the blood was negative with alcoholic antigen and positive with cholesterin antigen.

The patient was given 1200 c.c. of fluid a day. Calcium chloride, 15 gm. a day, was administered on 2 days. Increase in output of urine did not occur. It became necessary to remove fluid (1000 c.c.) from the right pleural cavity by paracentesis. Administration of digitalis, 1.3 gm. in 3 days, was followed by only a slight increase in output of urine. Fluid reaccumulated in the right pleural cavity, and 1200 c.c. of it were removed. Two weeks later calcium chloride was given again on 4 days; the administration of digitalis was continued, however. On the 4 days preceding the administration of calcium chloride the output of urine was 570 c.c., 782 c.c., 853 c.c., and 610 c.c., respectively. On the days it was given, the output rose to 886 c.c., 868 c.c., 1200 c.c., and 915 c.c. respectively. Diuretin and later theocin were given; no greater increase in output occurred than had resulted from the administration of calcium chloride. Calcium chloride was given again on 4 days. On this occasion increase in output did not occur. Although we were not able to induce diuresis by the usual measures, edema gradually diminished. Paroxysmal auricular fibrillation was often present. A hemorrhage, the origin of which was not discovered, occurred from the gastrointestinal tract. Later, strangulation of an inguinal hernia occurred, and the patient was removed to another hospital for operation. The patient died a few days later. An autopsy was not performed.

Summary.—In this patient there was severe cardiac decompensation. On two occasions the use of calcium chloride was without effect on the volume of urine. On another occasion, when combined with the use of digitalis, a slight increase occurred.

SUMMARY

Calcium chloride was given orally to six patients suffering from edema due to heart failure (Table I). Slight increase in the output of urine occurred, but marked diuresis was not observed. The administration of digitalis simultaneously with the oral administration of calcium chloride did not appear to be more effective than its use alone. The observations were repeated on several occasions on each patient. In two patients only was diuresis sufficient to free them of edema.

TABLE I

SUMMARY OF RESULTS FOLLOWING THE ADMINISTRATION OF CALCIUM CHLORIDE

CASE NO.	CALCIUM CHLORIDE				NUMBER OF OBSERVATIONS ON EACH PATIENT
	WITHOUT DIGITALIS		WITH DIGITALIS		
	DIURESIS	NO DIURESIS	DIURESIS	NO DIURESIS	
1	4*		3*		7
2	3*		3*		6
3				1	1
4				1	1
5		1			1
6	2*		1		3
TOTAL	9	1	7	2	19

*Refers to number of separate observations.

DISCUSSION

We have observed an increase in the output of urine following the oral administration of calcium chloride. Diuresis was never very marked, and in only two patients was it effective in decreasing edema. The results in even these two patients are contrary, however, to Blum's statement that the salt was without diuretic effect in edema due to heart failure. Nor did we observe deleterious effects following its administration. It may be recalled that Blum was of the opinion that cardiac patients do not tolerate the drug.

The mechanism by which calcium chloride acts as a diuretic is not known. Hjort[7] and Salvesen, Hastings and McIntosh[8] and others[4, 9] have found that the administration of it by mouth produces a severe uncompensated acidosis in dogs and in human subjects. This is due to a replacement of the HCO_3 radicle by Cl in the blood, as the result of absorption from the alimentary tract of the Cl of calcium chloride without Ca. There is an actual loss of base from the blood and a failure to adjust the carbon dioxide tension to the lowered bicarbonate. The calcium content of the blood serum may increase or may be unchanged. On the other hand the intravenous administration of calcium

chloride has no effect on the acid-base equilibrium of the blood; there occurs, however, a moderate rise in the phosphates. The injected calcium leaves the blood in from three to six hours. Whether the diuretic effect is dependent on the presence of the anion or upon the acidosis or upon some other mechanism is at present unsettled.

CONCLUSIONS

1. The administration of calcium chloride to cardiac patients with edema increases the volume of urine.

2. The increase in output which results is only occasionally effective in decreasing edema.

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OBSERVATIONS ON THE MECHANISM OF RELATIVELY SHORT INTERVALS IN VENTRICULOAURICULAR AND AURICULOVENTRICULAR SEQUENTIAL BEATS DURING HIGH GRADE HEART-BLOCK*

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A NUMBER of cases have been reported with electrocardiograms which displayed, in the presence of otherwise complete heart-block, ventriculoauricular sequences with brief intervals between ventricular and auricular contractions. The auricular elements of these sequences have been represented by abnormally shaped and usually inverted waves. Some observers have attributed these abnormal auricular beats to rapid retrograde transmission of the impulse. Thus Danielopolu and Danulesco[1] suggest that retrograde conduction may be preserved after forward conduction is lost, and they raise the question as to whether the pathways of forward and retrograde transmission may not be different. Veil and Codina-Altes[2] have recently also supported the hypothesis of retrograde conduction. On the other hand, Cohn and Fraser[3] proposed the hypothesis that the abnormal auricular beats are due to the mechanical stimulus of the contracting ventricular mass acting on auricular tissues. Wilson and Robinson[4] in discussing a case reported by them state that it must be assumed that ventricular systole hastened the discharge of a stimulus in the lower auricular or upper junctional tissues. Barker[5] who has recently written on this subject adopts a view which is essentially one of mechanical stimulation. He assumes that the contracting ventricle stimulates mechanically the His bundle above the lesion producing block and that the impulse is then transmitted in a retrograde manner through the A-V node to the auricles. These references are perhaps sufficient to indicate that the nature of the mechanism of retrograde sequential beats occurring during high grade heart-block is uncertain; no convincing evidence has thus far been produced.

The change back and forth in rhythm from otherwise complete heart-block to auriculoventricular sequential beating with normal transmission intervals has also been observed several times. In these cases the view seems to have been accepted by all writers on the subject that the sequential beats were due to transmission of the excitatory process through the junctional tissues. Carter and Dieuaide[6] believe that the

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bundle may contain only a few intact fibers which are just equal to the work of transmission under favorable circumstances but fail when stress occurs. The few cases of this nature in which anatomical study of the junctional tissues was subsequently made have all shown comparatively few fibers present capable of transmitting the impulse. The nature of the stress determining their failure to function at times is not known; possibly it is concerned with variations in blood supply to the bundle. We shall discuss this point later.

Our interest in these phenomena was aroused in 1922 by the finding, in a patient with otherwise complete dissociation, of isolated auriculoventricular and ventriculoauricular sequences having P-R and R-P intervals of approximately 0.16-0.17 second in the same strip of tracing. Frequent studies of this patient were made during the remaining five years of her life, and remarkable shifts back and forth among complete block, incomplete block and apparently normal rate of transmission were observed. Following her death, permission was granted to remove the heart; and serial sections of the bundle and of the upper part of the main branches were made. These studies are reported under Case 3 of our group.

We have encountered ventriculoauricular sequences with comparatively brief R-P intervals and abnormally shaped P-waves in the electrocardiograms of several cases of high grade heart-block and regard this finding to be much commoner than the literature suggests. In two of the cases the behavior was somewhat different from that of any previously reported and should be taken into account in the formulation of hypotheses to account for the mechanism of retrograde beats during high grade block.

CASE 1.—J. W., a man 60 years old, was admitted to the Medical Division of the Philadelphia General Hospital, Dec. 4, 1924, in a state of severe heart failure. There was present marked arteriosclerosis. The heart was greatly enlarged and showed evidences of aortic insufficiency. The rate was about 30 beats per minute and there were brief attacks of unconsciousness (Stokes-Adams syndrome).

An electrocardiogram made two days after admission (Fig. 1) showed a regular ventricular action of 28 beats per minute and an auricular rate of 50 beats per minute. The auricular rhythm was slightly irregular due to the fact that occasionally slightly premature ectopic auricular beats were in some way initiated by the preceding ventricular beat. In these sequences the R-P intervals measured approximately 0.16 second. The ectopic auricular beats were never highly premature occurring only late in the expected interauricular interval. In each instance the returning auricular cycle was slightly longer than those of the dominant auricular rhythm.

A tracing made six days later is shown in Fig. 2. At this time there was practically continuous coupling of ventricular beats. The first beat of each couple was of the usual idioventricular type, and the second was an extrasystole probably also arising in the junctional tissues. Both types of ventricular beats initiated premature ectopic auricular beats.

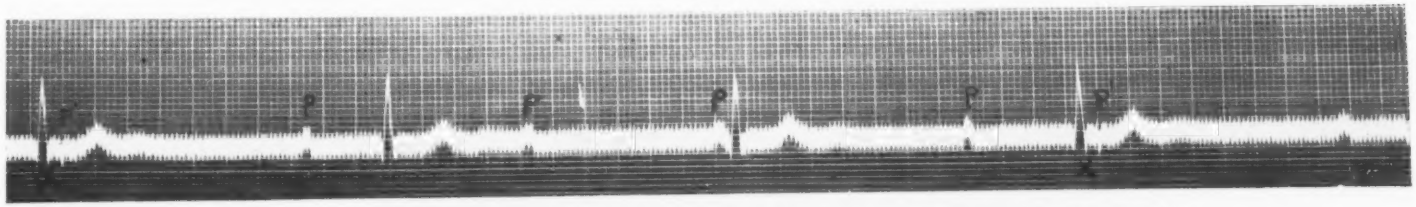

Fig. 1.—Case 1. Regular idioventricular rhythm, rate 28, with two ventriculoauricular sequences (*X*).

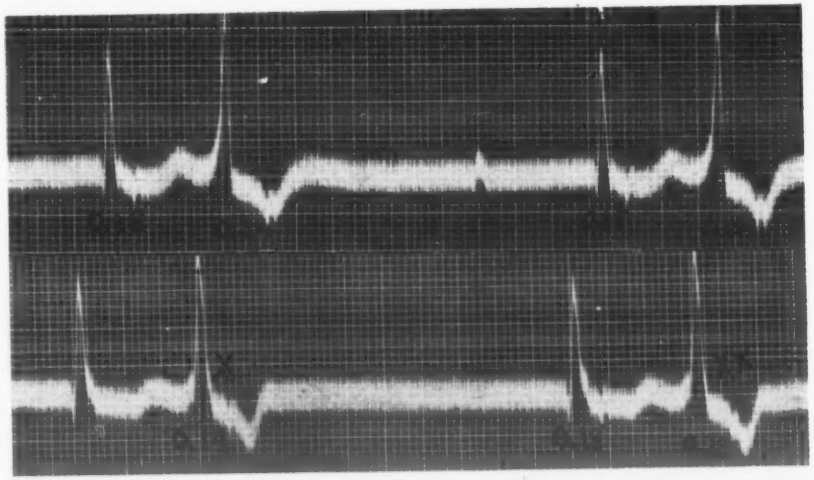

Fig. 2.—Case 1. Idioventricular rhythm with paired ventricular beats; each ventricular beat of the top strip forces auricular response. The R-P interval of the first sequence of each pair is 0.18 second, and the second sequence is 0.24 second. In strip 2, in the sequence marked *X*, the R-P interval is 0.19 second. The interval is shorter when the first ventricular beat of a pair does not force auricular response.

In strip 1, Fig. 2 (Lead II), the first sequential beat of the couples shows an R-P interval of approximately 0.18 second*, while the second sequence shows an R-P interval of 0.24 second. In strip 2, Fig. 2 (Lead III), there is no aberrant auricular beat following the first ventricular beat of the first couple. The sequence in connection with the second beat of the couple has an R-P interval of 0.19 second. In the following couple, both of which show ventriculoauricular sequences, the first R-P interval is 0.19 second and the second R-P interval 0.23 second.

COMMENT

Case 1 seems to furnish evidence bearing on the question as to whether the abnormal auricular beats of retrograde sequences are excited by mechanical stimulation or a transmitted (conducted), excitatory process. The fact that when two ventriculoauricular sequences occur in succession in connection with coupled ventricular beats, the second R-P interval is longer than the first suggests that the mechanism is one of conduction rather than mechanical stimulation. To this view, however, the objection might be raised that the differences in R-P intervals might be accounted for by the fact that the second ventricular beat was different mechanically from the first as shown by the altered electrocardiographic curve and the less time available for ventricular filling so that the mechanical stimulus to the auricle might be delayed. This objection is met by consideration of the effects of presence or absence of an R-P sequence in the first of coupled beats on the length of the R-P interval in the second beat of a couple as is shown in Fig. 2, strip 2.

It seems clear from these data that when two retrograde sequences occur as close together as 0.68 second there is a prolongation of the second sequence. This delay cannot be attributed to the fact that the second beat of the couple is premature, weak, or aberrant, since it does not occur when the first ventricular beat of the couple fails to force an auricular contraction.

We regard the above as strong evidence for the view that the abnormal auricular beats are stimulated by retrograde conduction of the excitatory process.† There is further evidence of a somewhat different nature. If one observes the time in the auricular cycle when the auricular element of the retrograde sequences occurs, it is found not only in our Case 1 but also in all cases we have studied and all tracings we have seen in published reports that they occur only late in

*These intervals were measured repeatedly with a Lucas comparator until a fair degree of consistency was obtained in the third decimal place. We therefore believe the figures to be accurate ± 0.005 second. The variations in transmission intervals pointed out are so wide, however, that high grade accuracy in measurement would not be necessary to determine them.

†It would seem out of the question to explain differences in R-P intervals of this magnitude by variations in latent intervals of auricular muscle. Available evidence seems to indicate that the latent interval of mammalian heart muscle is extremely brief.[7]

the expected interauricular interval.* It is precisely at such a time that the junctional tissues should be recovering their maximum functional capacity because of the lapse of time following the effort to transmit downward the preceding normal type of auricular beat. In connection with our Case 2 we shall attempt to show how a preceding period of unusually long rest in the bundle is followed by a relatively short ventriculoauricular sequence.

While the inexcitable period of junctional tissues, particularly if damaged, may be relatively long, that of auricular muscle is relatively short. There would thus seem to be no good reason, if the auricles were being excited by mechanical stimulation, why the responses should be limited to the latter part of the expected interauricular interval.†

One hesitates, in the present state of our knowledge, to accept an hypothesis assuming the occurrence of prompt retrograde conduction when forward conduction is either markedly delayed or fails com-

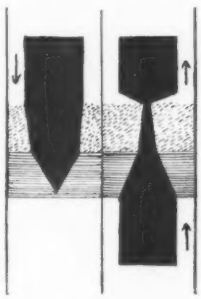

Fig. 3.—A diagram illustrating the conception of unidirectional transmission through junctional tissues. The solid black represents the excitatory process. As it descends (left) its vigor is impaired by a slight barrier to conduction (dotted area) just enough that it is unable to traverse a greater barrier (ruled area). The ascending (retrograde) excitatory process (right) meets the greater barrier before being subjected to decrement and is therefore able to pass it and avoid being blocked.

pletely, yet the data we have presented in Case 1 and shall present in Cases 2 and 3 demand its consideration. We find no precedent in the literature for such behavior, although so-called undirectional block from ventricles to auricles has been observed in several cases.[8] One can therefore only speculate as to the possible nature of a lesion permitting only unidirectional retrograde transmission. Conceivably it might be determined by the location of the chief barrier to conduction with reference to other secondary barriers. If we assume that the

*The incidence has been commented on by others. There is one apparent exception found in a tracing published by Danielopolu and Danulesco[4] during vagal stimulation in which an inverted P-wave of the type under discussion occurred shortly after a normal P-wave. In this case, however, there was said to be no conduction defect. Under such circumstances escape from vagal inhibition might readily have permitted transmission to occur.

†The chief objection to the compromise hypothesis of Barker[5], to the effect that the ventricles mechanically stimulate the junctional tissues above the area of block whence the impulse is carried to the auricles in a retrograde direction through the A-V node, is the short R-P intervals. There would not seem to be time for the occurrence of this double mechanism.

descending excitatory process is subjected to decrement in its downward path, it might be unable to traverse the final most serious obstacle whereas an excitation from below might be able to traverse the serious obstacle and be transmitted through the less important barriers to conduction. The point may perhaps be made clearer by the analogy to a runner who might be able to jump a broad stream at the beginning of his race and then overcome relatively minor obstacles, whereas if the minor obstacles had come first he might have been so fatigued as to be unable to jump the broad stream.

In Fig. 3 we have attempted to diagram this conception of unidirectional transmission.

CASE 2.—Mrs. F., 37 years of age, was referred for examination, June 23, 1923, to the Heart Station of the University Hospital. She had consulted her physician because of attacks of vertigo. He, noting that the pulse was slow and somewhat irregular, requested an electrocardiogram.

The tracing (Fig. 4) shows two-to-one heart-block. There are present two types of auricular arrhythmia. One of them is a form of sinus arrhythmia, the auricular cycles which contain QRS complexes tending to be shorter. The other form of auricular arrhythmia is due to fairly frequent premature ectopic beats following ventricular beats. These ectopic beats, as in Case 1 are found only toward the latter end of the expected auricular cycle. The R-P intervals are all approximately 0.26 second in duration except the R-P interval found after a premature beat (*X*) which is 0.22 second.

COMMENT

In Case 2 two modes of stimulation suggest themselves as possible mechanisms by which the ectopic auricular beats are excited: (1) reciprocating beats, and (2) mechanical stimulation.

Mines[9] in 1913 described an abnormal mechanism which he was able to produce by rhythmic stimulation of the heart of the electric ray and the frog, which he called reciprocating rhythm. The rhythm of each chamber (auricle or ventricle) seemed to be dependent on the other, and the alternate contractions spaced approximately evenly would continue for long periods unless interrupted by a stimulus. The mechanism could be initiated by an extrasystole or when already present stopped by an extrasystole. Mines regarded the condition as a circulating mechanism. He offered the suggestion that under rapid stimulation different fibers would recover at different rates and the impulse going in one direction through certain fibers would go in the opposite direction through other fibers.

White[10] and Drury[11] have reported clinical cases which appear to be examples of reciprocating beats and Drury has called attention to the similarity of the mechanism in his case with that produced experimentally by Mines. In their cases, however, the impulse apparently arose in the junctional tissues and spread to both ventricles and auricles. When conduction was strained so that the auricular beat was delayed, an impulse would descend to the ventricles and a second

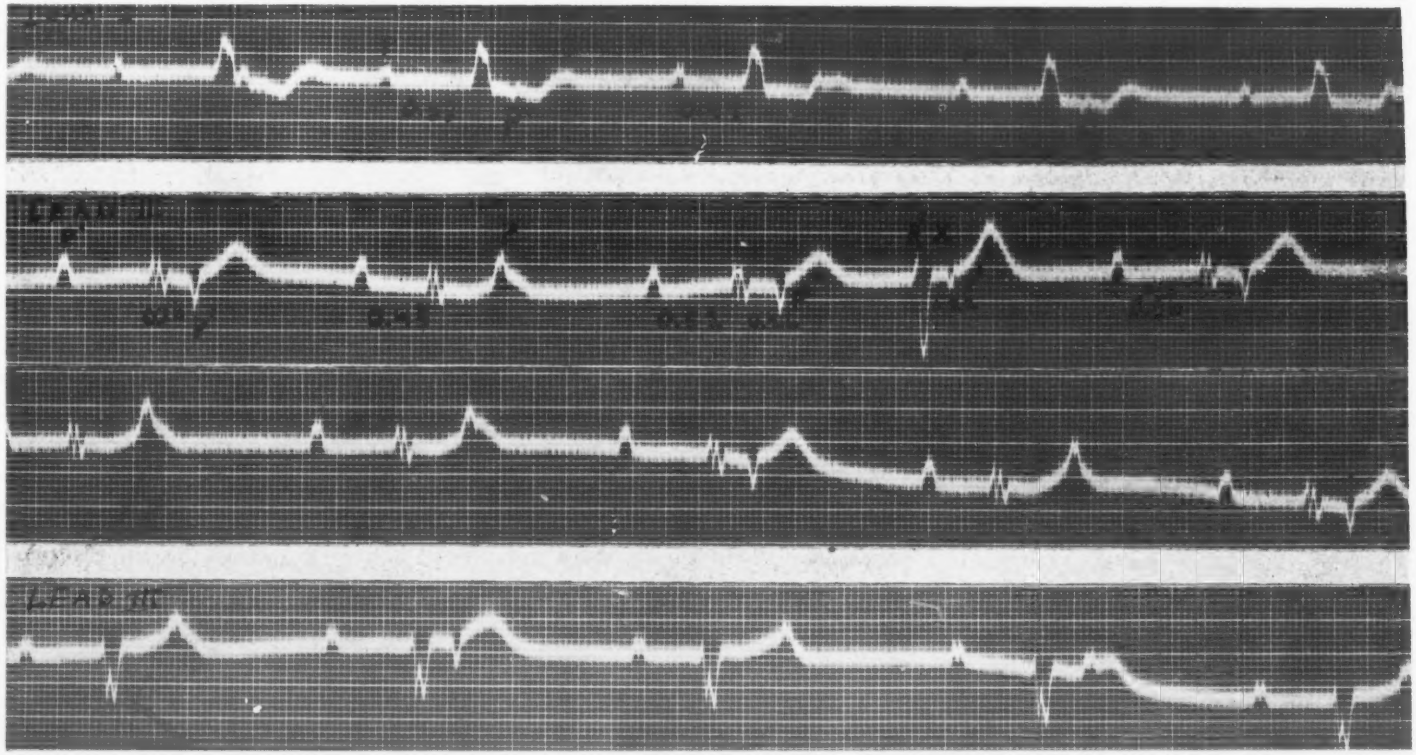

Fig. 4.—Case 2. Two-to-one heart-block. Reciprocal beats each with a sequence consisting of normal type auricular beat, long P-R interval (0.52-0.56 second), ventricular beat, R-P interval of 0.26 second and ectopic auricular beat.

The R^1-P^1 interval in connection with the premature ventricular beat in Lead II (*X*) is 0.22 second. This aberrant auricular wave is not so deeply inverted as the others. It falls just at the time a normal auricular wave is expected and probably inscribes the combination of a normal beat spreading from the sino-auricular region plus the ectopic beat.

ventricular beat occur. Gallavardin and Gravier[12] demonstrated in a case of A-V nodal bradycardia that by vagal stimulation and thus lengthening R-P intervals, reciprocating beats could be produced. Scherf and Shookloff[13] have recently made an experimental study of reciprocating beats (umkehr Extrasystolen) and believe the site of reversal to be in the upper part of the nodal tissue. So far as we are aware no clinical case has been described previously in which the course of the reciprocating beats was from auricle to ventricle back to auricle again. In our case it is obvious that conduction was in a critical condition, the state insisted on by most workers as necessary for the production of reciprocating rhythm. The one objection, so far as we are aware, which may be raised against this interpretation is the fact that retrograde transmission must be assumed to proceed more rapidly than forward transmission. It has been shown repeatedly in experiments that conduction is more readily accomplished from auricles to ventricles than from ventricles to auricles and that A-V intervals

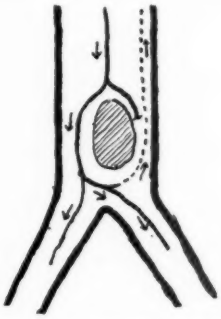

Fig. 5.—A diagram illustrating the conception of reciprocal beats in Case 2. The oval ruled area represents a lesion in the bundle of such a character as to cause the formation of two pathways, both offering obstacles to conduction but the one on the right more than on the left. Each alternate descending impulse is transmitted down the left side but is blocked on the right. The left descending impulse after passing the lesion spreads not only to the ventricles but also upward on the right side of the lesion. Some of these impulses are transmitted back to the auricles. The successful retrograde transmission is due either to (1) longer recovery period due to block of descending impulse on right side or (2) position of barriers to conduction permitting only unidirectional (in this case, retrograde) transmission. See Fig. 3.

tend to be shorter than V-A intervals. However, the evidence presented in our Case 1 which seems to indicate that in at least one case retrograde transmission has been successfully accomplished even though forward conduction from auricles to ventricles was lost, justifies consideration of the possibility that in lesser grades of block, A-V intervals might exceed V-A intervals. Any alternative hypothesis would seem to involve the assumption of mechanical stimulation of auricles by contracting ventricles. To this view there are the following objections:

1. The incidence of the ectopic auricular beats is always late in the auricular cycle. The significance of this fact in its relationship to the relative probability of transmission or mechanical stimulation has already been discussed in the presentation of Case 1.

2. The R-P intervals are much longer than in any of the cases in which mechanical stimulation was proposed as the mechanism. One must therefore assume that the mechanical stimulation has in some way been delayed. In view of the unusually long forward transmission intervals, however, one might reasonably expect delayed retrograde transmission also.

3. We are unable to account for the shorter R-P interval after an extrasystole (*X* in Fig. 4) on the basis of mechanical stimulation. It is readily accounted for on the basis of retrograde transmission since the rest period preceding this beat is decidedly longer than any others preceding ectopic auricular beats. The longer rest period may therefore account for accelerated transmission of the next beat.

For these reasons the hypothesis of mechanical stimulation seems inapplicable to this case; and we, therefore, favor the interpretation of a circulating mechanism similar to that proposed by Mines. It is probable, however, that in the clinical cases the mechanism is not identical with that observed by Mines, since continuous transmission back and forth between auricles and ventricles has not been observed. Possibly in such a case as ours the mechanism is due to peculiarity in the location of a lesion in the bundle resulting in two pathways with slightly unequal conductive capacity joined above and below the lesion in such a way that a circulation of the excitation could occur (Fig. 5).

CASE 3.—Mrs. A. H. S., a white woman, 48 years old, was admitted to the Medical Division of the University Hospital Sept. 8, 1923, complaining of "thumping of the heart." The history dated back to 1912 when she had an attack of syncope with nausea and vomiting. At that time she was informed that she had a weak heart. In 1914 she was told that her heart rate was unusually slow. During the following years the slow rate (usually about 30 beats per minute but sometimes as low as 13 beats) had occasionally recurred. Since January, 1923, her difficulties had increased markedly. She was bothered by almost constant thumping of the heart, pain and sense of constriction in the chest, frequent attacks of vertigo and occasional syncope. In the spring she entered the Lankenau Hospital and was told that she had heart-block, although no electrocardiograms were made. During the summer she was admitted to the Philadelphia General Hospital. At this time electrocardiograms showed the presence at times of complete heart-block, and at other times various manifestations of incomplete block.

The past medical history is unimportant except for the suspicion of tuberculosis in 1914, but studies carried out in a sanatorium were negative. Her habits have always been good. She has always done housework with occasional short periods of work in a mill. Her father is said to have died of heart disease, her mother of apoplexy, and of 7 siblings, one brother has heart disease and two sisters have had tuberculosis. Two of her three children are said to have heart disease.

Physical Examination.—The patient was a sallow, poorly nourished woman who looked older than her stated age. She was obviously weak but able to walk about the ward. Nearly all teeth were missing. The tonsils were small and innocent in appearance. The thyroid was slightly enlarged. The lungs showed evidences of an old lesion at the right apex. The heart was not enlarged. The rate was 30 beats per minute and the rhythm regular. There was a systolic apical murmur,

and in the third interspace to the left of the sternum a distinct short sound was heard about midway between beats. The peripheral arteries appeared to be in good condition, and the retinal vessels showed no abnormality. The blood pressure was 135/70 mm. The liver was enlarged, extending 8 cm. below the costal margin in the midclavicular line. The spleen was barely palpable.

Several blood counts were normal. All blood Wassermann tests were negative. The urine showed traces of albumin and hyaline casts from time to time but was otherwise negative.

On the first admission to the University Hospital the patient remained in the ward from Sept. 8, 1923, to Dec. 23, 1923. During this time she showed wide variations in cardiac behavior. There was a period of several days during which complete dissociation was present. No drugs had been taken prior to this period of block. On one occasion there was an attack of syncope which developed while she was being examined. The radial pulse disappeared entirely, and no heart sounds were heard. An intracardiac injection of epinephrin was ordered, but

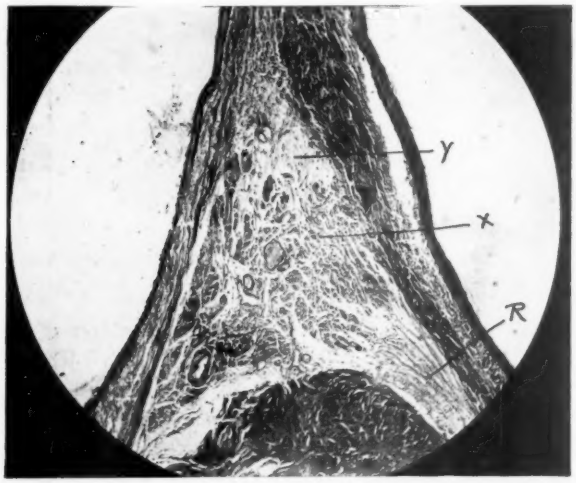

Fig. 6.—Shows the main bundle of His (*X*) and the right branch (*R*). In the upper portion of the main bundle is shown a defect (*y*).

just as it was to be given heart sounds and pulse reappeared. A second, apparently similar attack occurred during the night.

Usually the mechanism was 2-to-1 block, at other times 3-to-1, 3-to-2, and for long periods no block would be apparent. Rates as high as 140 beats per minute were observed with all beats transmitted. Prolongation of transmission intervals was never observed.

There were four subsequent admissions to the University Hospital. While she was at home, she was under the care of one of us. Consequently she was under fairly close observation for over five years. It was observed that marked bradycardia always caused a great deal of distress, and this was the reason for each admission to the hospital. On the first three admissions the block disappeared after varying periods of complete rest. On the fourth admission barium chloride seemed to help abolish the block. The final admission was on Dec. 13, 1927. This time the idioventricular rhythm persisted in spite of treatment (complete rest and barium chloride); the rate grew progressively slower, and the circulation seemed to fail more or less proportionately. Death occurred Jan. 10, 1928.

Permission for necropsy was limited to the heart. Nothing noteworthy was discovered on gross examination except a small area of fibrosis in the septum centering about the region of the branching of the bundle. The heart was not enlarged; there were no pericardial adhesions and no valvular defects. The larger coronary vessels showed some evidences of arteriosclerosis, though at no point, so far as gross dissection revealed, was the lumen encroached upon.

Histological Studies of Junctional Structures

The block of tissue sectioned serially included the conducting tissue from the lower portion of the A-V node to well beyond the point of division of the main bundle into its two branches.

The A-V node and the upper half of the main bundle were relatively normal histologically. Approximately half-way down the main bundle a small area of round-cell infiltration appeared. From this point on, the main bundle became increasingly pathological, there being more and more interstitial fibrosis and several minute areas of beginning calcification. The small ramifications of the coronary

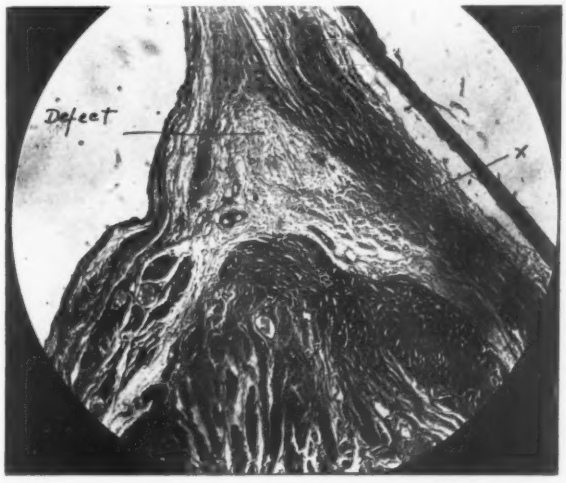

Fig. 7.—Shows the same area further forward. The whole of the main bundle is replaced by the defect, only one small area of muscle (*X*) being seen.

arteries showed thickening, this going to the point of practical occlusion in some instances. In spite of the pathological condition of this region of the bundle the individual muscle fibers appeared relatively good.

When the region of the division of the main bundle into its branches was approached, not only were changes of the same order still in evidence but also there appeared a degenerative lesion that resulted in destruction of the involved portions.

This lesion was conical in shape with its apex pointing posteriorly. Studying this portion of the bundle from behind forward, approximately the first eighth of its diameter presented the same appearance as the higher levels; namely, fairly healthy individual muscle fibers in the midst of greatly increased interstitial fibrous tissue. Further in front of this posterior eighth of the bundle the apex of the destructive lesion appeared. This enlarged in all directions conically as the front of the bundle was approached. As the lesion became extensive, it dipped well down into the anterior portion of the right branch. The left was not involved.

The lesion itself showed a complete absence of muscle fibers, and in their stead was seen a reticulum of large rounded spaces that apparently were the re-

mains of fat cells, the fat itself having been dissolved out in the process of fixation.

The condition of the right branch remains to be described. The large lesion of the main bundle dipped down into this branch in its anterior portion and destroyed it for a definite distance. In the posterior portion of the right branch, another lesion, apparently independent but probably of the same nature, was present. The section here happened to show the fibers cut absolutely longitudinally. The muscle fibers were entirely gone with only a fibrous reticulum remaining, giving the appearance of the strings of a harp. The nature of the degenerative lesion that resulted in this appearance seemed doubtful to us. Perhaps a fatty change, similar to that causing the big lesion of the main branch is the most likely explanation (Figs. 6, 7 and 8 show the destructive lesion in the main bundle).

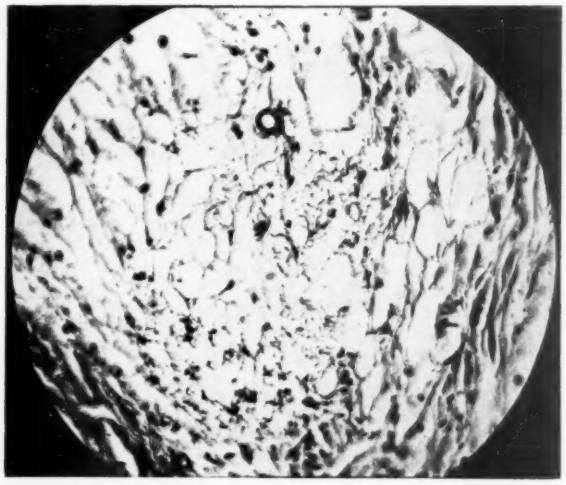

Fig. 8.—Is a high-power photomicrograph taken from the same area. The muscle fibers in this area are completely gone except for a small group of fibers in the lower left corner of the illustration. In place of the muscle fibers are large empty spaces enclosed by a reticulum of fibrous tissue that are presumed to have contained fat.

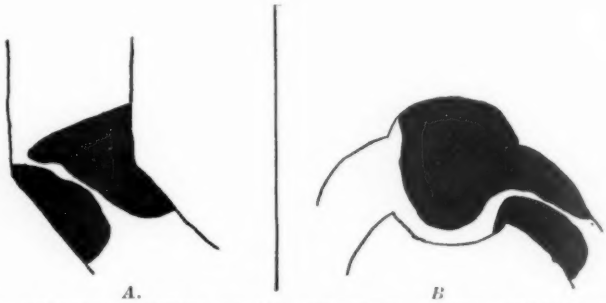

Fig. 9.—A schematic drawing of the destructive lesions (shaded) in the main bundle and its right branch. *A*, lateral view of main bundle and right branch; *B*, looking down on main bundle and branches.

The two lesions in this branch, one anteriorly and one posteriorly, almost came together. However, between the two there were relatively few strands of conducting muscle. These fibers were distinctly atrophic, stained poorly and were clearly far from normal. However, we believe that under certain conditions these fibers did successfully transmit impulses.

Summary of Findings.—There was a lesion of the main bundle that completely destroyed those portions involved. This lesion failed to involve an area of the bundle on the left side and posteriorly equaling approximately one-eighth of the total diameter of the bundle. Furthermore, the lesion being conical in shape, resulted in there being slightly more undestroyed tissue around its narrowed apex than around the wider base. However, the narrow band of undestroyed bundle was the seat of round-cell infiltration, areas of early calcification, arterial disease and increased fibrosis. These changes resulted in individual groups of muscle fibers being so separated from other groups that it seems quite probable to us that conduction was interrupted.

The right branch showed complete destruction except in its central portion where a relatively few fibers that were definitely diseased probably afforded a path of conduction under certain circumstances at least. (Fig. 9 is a schematic representation of the destructive lesion in the main bundle and its right branch.)

Description of Electrocardiograms

We have selected from the numerous tracings made, only those which seem to be representative of peculiar variations in mechanism observed.

The tracing in Fig. 10 shows complete dissociation, occasionally interrupted by slightly premature ventricular beats (*X*) each bearing an exact relationship to the preceding auricular beat and obviously excited by the auricular beat. These premature ventricular beats are all aberrant in form. There is also found some auricular arrhythmia due to slightly premature aberrant auricular beats (*XX*) each bearing a relationship to the preceding ventricular beat and obviously excited by it. The P-R intervals are 0.15 second and the R-P intervals 0.16 second. The premature auricular beats are similar in type to those recorded in Cases 1 and 2, but the R-P intervals are shorter than those found in Case 2.

That the aberrance of the ventricular beats excited by auricular contractions is not due to their prematurity is shown in Fig. 11 in which two highly premature beats (*X*) are found to have normal type complexes. These two beats are probably junctional extrasystoles arising below the level of the block. This view is favored by the fact that they are accurately coupled with preceding ventricular beats and not with auricular beats.

In Fig. 12 there are shown various manifestations of sequential beating. In strip 1 is seen the end of a paroxysm of auricular tachycardia in which all auricular beats stimulated ventricular response. In strip 2, there is 3-to-2 block, in strip 3, 2-to-1 block and in strip 4, 3-to-1 block.

In Fig. 13 we see the shift from 2-to-1 rhythm to complete dissociation. The first three ventricular beats recorded are aberrant as always occurred with sequential beating. The P-R intervals were approximately 0.16 second. At the fourth ventricular beat ventricular escape begins to assert itself, and by the sixth beat it is complete. The fourth and fifth beats are transition forms.

Effect of Vagus Stimulation.—Vagus stimulation was tried many times during periods of incomplete block. The methods employed were pressure on either right or left vagus in the neck, pressure on both sides simultaneously and ocular pressure. The auricular rate could be slowed by vagus stimulation, but on no occasion did higher grade block result.

Effect of Drugs.—Repeated intramuscular injections of atropin were made with electrocardiograms taken just before injection and every fifteen minutes up to from two to three hours after injection. The dosage employed was usually 3 mg. of atropin sulphate, but twice during periods of 2-to-1 rhythm 6 mg. were used.

Atropin in these dosages invariably caused acceleration of the auricular rate. Associated with this acceleration, an original 1-to-1 sequential rhythm might be

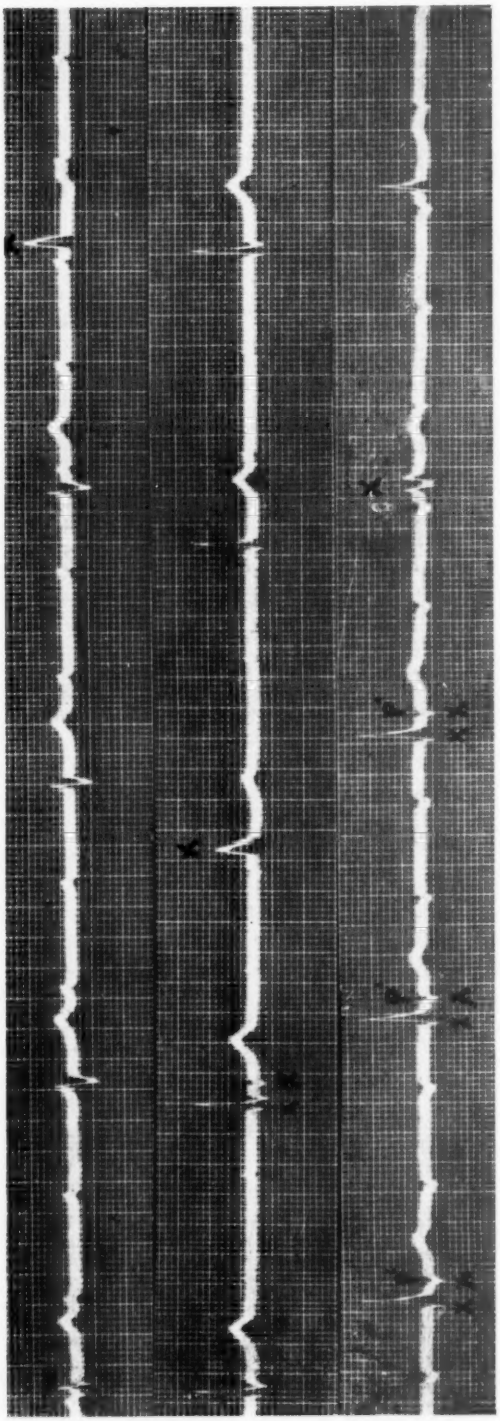

Fig. 10.—Case 3. High grade heart-block with isolated brief auriculoventricular sequences (marked with *x* above) and brief ventricular sequences (marked with *xx* below). In the A-V sequences the ventricular complexes are invariably aberrant, and in the V-A sequences the auricular complexes are aberrant.

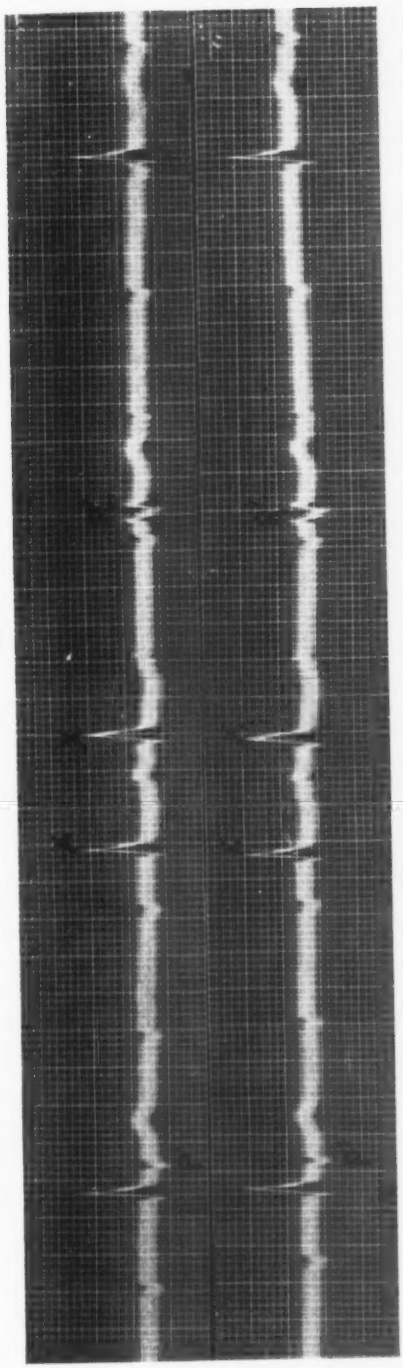

Fig. 11.—Case 3. The tracing shows that aberrant ventricular complexes in A-V sequences are not due to their slight prematurity since highly premature ventricular complexes have the normal form.

converted to 3-to-2, 2-to-1, or even 3-to-1 rhythm. An original 2-to-1 rhythm usually remained unchanged in spite of acceleration of auricular rate, although occasionally 3-to-1 rhythm resulted.

During periods of complete dissociation atropin sulphate in dosage of 3 mg. did not change the rhythm to the sequential type in either of two experiments. A third test was made when dissociation was almost but not quite complete (May 26, 1925), there being but occasional isolated sequential beats and a few short runs of 2-to-1 rhythm. Following the injection the usual auricular acceleration occurred and no more runs of 2-to-1 rhythm were observed although there were still isolated sequential beats.

These studies seemed to us to demonstrate beyond question that atropin showed no tendency to lessen block. Under its use the grade of block showed a tendency

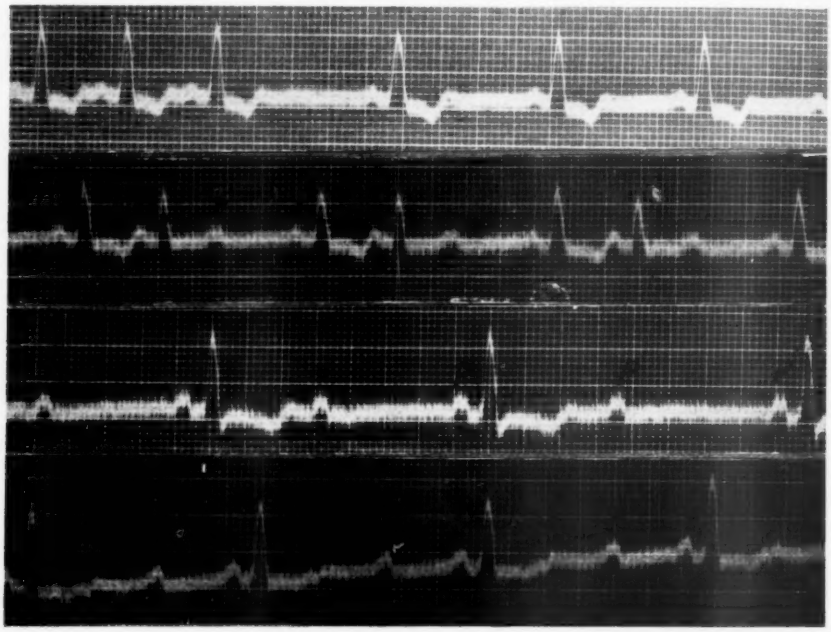

Fig. 12.—Case 3. Top strip shows end of a period of tachycardia in which there had been no block. Second strip shows 3-to-2 block; third strip, 2-to-1 block; and fourth strip, 3-to-1 block. All P-R intervals are well within normal limits. Such variations as are noted here occurred within periods of a few days.

to increase, probably due to acceleration of auricular rate rather than to any actual increased difficulty in conduction.

The effects of amyl nitrite are seen in Fig. 14. The effects seem to be quite identical with those of atropin except for the fact that they run their course over a period of a few minutes rather than hours. Like atropin the apparent increase in block is probably due merely to auricular acceleration.

Only one experiment was made with epinephrin because the drug caused very unpleasant pounding of the heart. On May 27, 1925, during a period of 2-to-1 rhythm intramuscular injection of 0.5 c.c. of a 1-1000 solution of epinephrin accelerated the auricular rate but failed to disturb the 2-to-1 rhythm.

The patient was rather intolerant of digitalis and nausea and vomiting tended to occur after 1 to 1.2 gram of digitan. Three experiments were made during periods of sequential beating in the attempt to convert the mechanism to com-

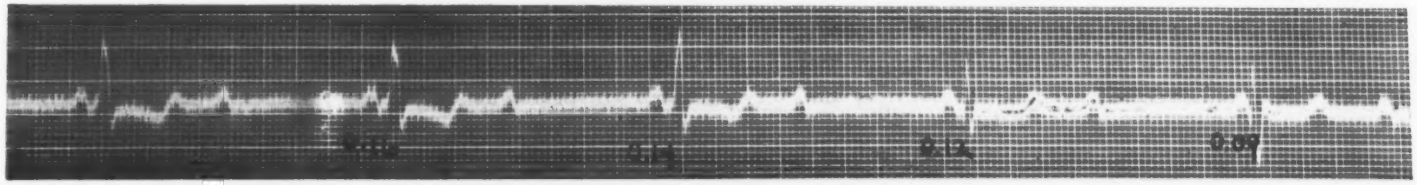

Fig. 13.—Case 3. Transition from 2-to-1 block to idioventricular rhythm. This is accomplished here by escape of the idioventricular center. Gradual change in form of ventricular complexes as the idioventricular center gradually gains control.

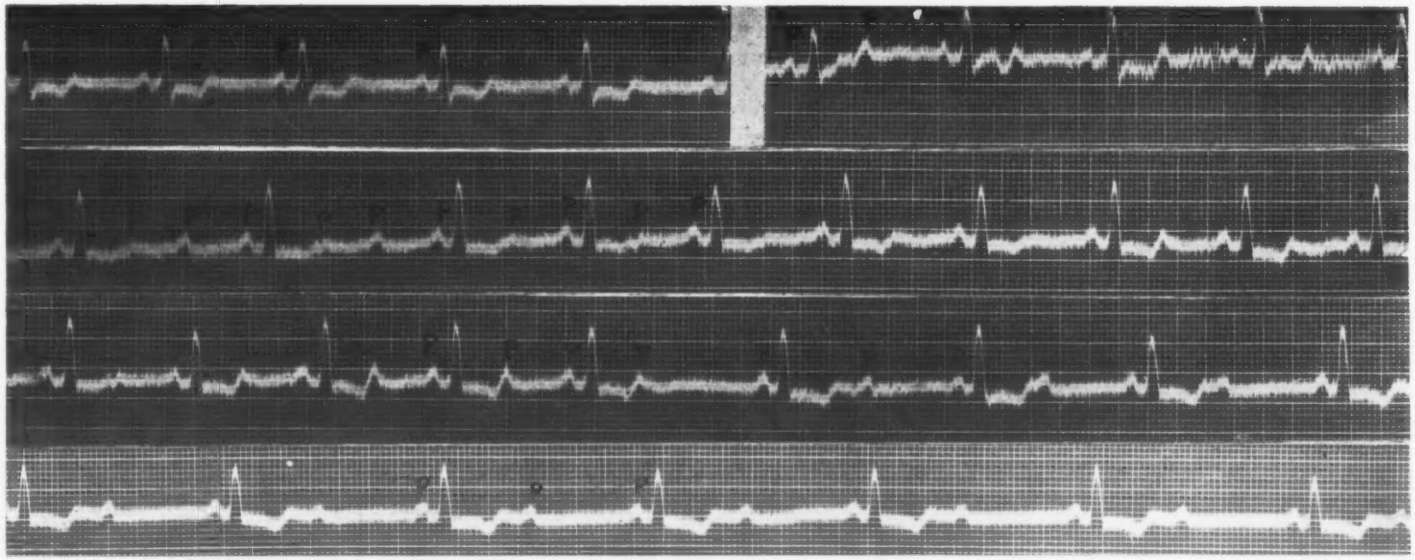

Fig. 14.—Selected strips of tracing before, during, and after amyl nitrite inhalation showing change from normal rhythm as the auricular rate accelerated to 2-to-1, then 3-to-1 block. As the auricular rate began to slow, 2-to-1 block returned and persisted for a long time after the conclusion of the experiment. All P-R intervals are approximately constant and well within normal limits.

plete dissociation. The method used was administration by mouth of 0.13 gram of digitan t.i.d. to the point of vomiting which occurred on the third day. This occurred whether she did or did not know she was receiving digitalis. Twice no effect was noted on the sequential rhythm, but on the third attempt dissociation resulted about the time vomiting began. Because of the tendency to spontaneous change back and forth between sequential beating and complete dissociation, we did not feel justified in concluding that digitalis had been responsible for the change observed. The following morning after a few doses of barium chloride had been taken, there was 1-to-1 rhythm with no evidence of block. It therefore seemed possible that the shift to complete dissociation during this one of three trials with digitalis might have been accidental or at most evidence of a very feeble digitalis effect.

Barium chloride* was found for a long time to have a distinct effect in abolishing block and restoring 1-to-1 rhythm. Finally, however, it seemed to lose its effectiveness, at least in the dosage employed (20 mg., q.i.d.) We did not increase the dosage because of the production of ectopic ventricular beats singly and in series.

DISCUSSION

The Ventriculoauricular Sequential Beats.—A most instructive case has been reported by Krumbhaar[14] in which, despite the presence during life of complete heart-block, serial sections of the bundle showed comparatively little damage to the junctional tissues. In our Case 3 the presence of complete heart-block for quite some time before death suggested that complete destruction of the bundle at some point had occurred. Nevertheless, it was found that at the level of greatest damage approximately one-eighth of the bundle had apparently remained fairly intact. While these fibers had failed to transmit impulses for quite some time, probably several months, the histological findings suggested that there might have been ample muscle tissue present to conduct an impulse.

There is clinical evidence to indicate that complete block may be present for months without permanent loss of the ability to transmit impulses. One of us has observed a patient who showed complete heart-block in all examinations made during a period of six months but temporarily resumed normal rhythm with normal P-R intervals after eradication of extensive oral infection (unpublished case).

Findings of this type demonstrate the danger in assuming, because block has persisted for a relatively long time, that the ability to transmit impulses has been permanently lost. Furthermore, the assumption that if the ability to transmit impulses from auricles to ventricles is lost even transiently retrograde conduction must also be lost, is on equally uncertain ground. The possibility of unidirectional transmission cannot be excluded. Nevertheless on these foundations rests the reasoning which has led to the hypothesis of

*Studies of the action of barium chloride in this patient have been made the subject of a separate communication. (J. Lab. & Clin. Med. In Press.)

mechanical stimulation as the mechanism of retrograde beats in otherwise complete heart-block.

The data obtained in Case 3, so far as we are able to analyze it, offers no evidence in favor of mechanical stimulation of auricles by ventricles. It does, however, offer the following evidence in favor of retrograde transmission as the cause of the abnormal auricular beats although none of the points could be regarded as conclusive.

1. Retrograde sequences occurred only at such times as forward transmission was in evidence. If the retrograde sequences were due to mechanical stimulation, there would seem to be no good reason why they should not have occurred quite as readily at times when complete dissociation was established.

2. The P-R intervals and R-P intervals were approximately of the same length.

3. As in all other cases observed the R-P sequences occurred only in the latter part of the auricular cycles. The significance of this finding has been discussed above.

It seems to us, therefore, that the evidence we have been able to furnish in our three cases, supports in different ways the view that rapid retrograde sequences in the presence of high-grade or supposedly complete heart-block are due to retrograde conduction through the junctional tissues. It is opposed to the hypothesis of mechanical stimulation.* Furthermore the data supplied in connection with the cases previously published in support of the hypothesis of mechanical stimulation are not convincing.

Intermittent Heart-Block.—Wells and Wiltshire[15] have described a case in which intermittent complete heart-block was observed over a period of twelve years. Between attacks the transmission intervals were normal. At necropsy an area of calcification was found involving the A-V node, but continuity of muscle fibers in the bundle was apparently preserved.

In our Case 3 it is probable that intermittent complete block had lasted over a period as long as fourteen years although no electrocardiograms were made until five years before death.

Intermittent complete block is rare, and but few cases have been reported. The condition has been recently reviewed by Carter and Dieuaide[6].

Intermittent incomplete block with normal transmission intervals is not nearly so rare, and we as well as others have obtained records of a number of cases showing principally 2-to-1 block. The present

*We have failed in the attempt to force auricular contractions by mechanical stimulation from the ventricles in the dog. The method used was as follows: The dog was anesthetized by ether and an intratracheal respiration apparatus introduced. The thorax was opened, the pericardium incised, and a Lewis clamp applied to the junctional area so that complete heart-block was produced. Connection was then made between auricles and ventricles by means of a thread in the attempt to make a mechanical pull from the contracting ventricle to the auricle force auricular response. This was tried in many locations and with varying tensions of the thread but without success.

case shows the essential similarity in mechanism between intermittent incomplete and complete block, since numerous transitions occurred among normal rhythm, incomplete block with normal transmission intervals and complete block.

Carter and Dieuaide point out that there is indicated in intermittent complete block a progressive anatomical lesion of the auriculoventricular bundle and thus a tendency toward the establishment of permanent block. In this connection it is of interest to note in our Case 3 that the final period of complete block had probably lasted for several months preceding death and that the isthmus of relatively intact muscle in the bundle showing round-cell infiltration suggested progression in the lesion. Round-cell infiltration was also present in the bundle in Wells and Wiltshire's case.

It is possibly of some interest to speculate on the nature of a lesion that may permit sudden transitions back and forth between complete block and normal rhythm. Carter and Dieuaide's suggestion that the bundle contains only a few intact fibers which are just equal to the work of transmission under favorable circumstances but fail when stresses occur does not offer an explanation as to why in some cases of high-grade heart-block all transmitted beats have normal P-R intervals. The findings in our case suggest that the important factor may be the length of the critical area, in other words the distance through which the excitation must traverse damaged tissues.

Lewis[16] has proposed the view that prolongation of transmission intervals is due to the distribution of unexcitable tissue in the bundle in such a way as to require the excitatory process to pursue a sinuous course. Thus, if the barrier to conduction is short, it is easily conceivable that such impulses as are able to pass do so with little delay since little or no deflection from a straight course would occur.

Number and Condition of Fibers Capable of Conducting the Excitatory Process.—Factors which determine whether conduction or block of the excitatory process is to occur are not clearly understood. If the generally accepted view is correct, namely, that the excitatory process is an electrical disturbance transmitted from muscle fiber to muscle fiber, it would seem possible that continuity of single intact fibers might be sufficient to transmit the impulse effectively. It has been stated that a few fibers are capable of transmitting the impulse. Nevertheless, it is well known that conduction may fail despite the fact, that, as was shown in Krumbhaar's case,[14] later anatomical studies show abundant continuity of fibers which so far as can be told from their histological appearances should be capable of function.

Our Case 3 affords a very striking example of this apparent paradox. Transmission of the excitatory process frequently failed in the

main bundle, and during the last period of study before death transmission was not recorded despite the fact that serial sections of the bundle later showed that approximately one-eighth of the muscle was still present although doubtless somewhat damaged.

On the other hand, during periods of complete heart-block, the shape and duration of the QRS complexes of the electrocardiogram indicated that the impulses were spreading to the ventricles in a normal manner. From this we are compelled to assume that the impulse passed down not only the left main branch but also the right main branch as well. A tracing made three days before death still showed the normal type of QRS complexes. In spite of this finding the serial sections of the right branch showed that at one level destruction was complete except for a few atrophied fibers less than one-half the normal diameter. We must then conclude that these few greatly atrophied fibers conducted the excitatory process through the right main branch without appreciable delay. We are entirely unable to offer any explanation as to why on the one hand a mass of fibers relatively intact failed to function whereas a little lower a few greatly atrophied fibers apparently functioned normally. The natural inclination would be to question the data. Concerning the tracings there can be no question, and the sections have been studied so exhaustively as to seem to admit of no doubt as to correctness of the findings.

The Failure of Drugs and Vagus Stimulation to Effect the Degree of Block.—The response to atropin in the few cases of intermittent complete heart-block tested has been variable. In some previous cases it has been without effect. Carter and Dieuaide therefore repeat the previous warning of Lewis to the effect that atropin is not conclusive as to the pathogenesis of heart-block. In other words, the failure of atropin to relieve or decrease block does not exclude the possibility of a functional element being present, as opposed to anatomical loss of continuity in the bundle. This view our case abundantly confirms.

The description of our atropin experiments given above would seem to exclude the likelihood of vagus effect being concerned in the block. The most decisive experiment in this respect is regarded by us as the injection of atropin made when block was not quite complete. This should have been a peculiarly favorable time at which to demonstrate vagus effect yet none could be obtained.

The fact that during one-to-one transmission or various forms of incomplete block vagus stimulation was without effect in increasing block is further evidence of the absence of vagus effect. The uncertain or at most feeble effect of digitalis might also be interpreted as due in part to absence of vagus effect in the block.

The failure of amyl nitrite and our one experiment with epinephrin suggest that accelerator influences were also without effect.

From these experiments we conclude that nervous influences, either vagus or accelerator, were either entirely lost or so feeble as to be of no importance in the area of block.

It is of interest to note the effect of auricular rate on the grade of incomplete block. The results whether produced by amyl nitrite or by atropin were similar and may be seen in Fig. 14. As auricular rate was increased, there was a tendency for block to increase; and as the auricular rate declined, the grade of block declined. Thus in the course of a few minutes under the influence of amyl nitrite there was obtained 1-to-1, 2-to-1, 3-to-1, and 2-to-1 beating.

Barium chloride was the only drug which showed definite effect in abolishing block, although it finally lost its effect. Since barium is supposed to exert its effect by increasing excitability, we assume that this action was produced in the critical area. The final loss of this effect might have been due to the diminution of blood supply. An examination of the arterial twigs showed so much thickening and encroachment on the lumina of the vessels that the blood supply must have been precarious.

Aberrance of QRS Complexes of Sequential Beats.—Slight differences in shape between the ventricular complexes of idioventricular and transmitted beats are not uncommon. One of us has recently reported a case in which each type of beat has its characteristic QRS complex[17]. We have not, however, previously seen tracings in which the QRS complexes of transmitted beats were decidedly aberrant in form while those of idioventricular beats were within normal limits.

The degree of aberrance recorded in the ventricular waves of the transmitted beats is not sufficient to represent a complete bundle-branch block. It does, however, indicate some irregularity in the spread of the excitatory process through the ventricles. Nevertheless, the fact that idioventricular beats inscribe normal ventricular complexes suggested that the fault did not lie in either of the branches but was to be found above the idioventricular center.

The studies of the junctional tissues suggest that the explanation for the two types of ventricular curves is concerned with the position of the largest lesion. Fig. 9 shows that it lies mainly on the right side and dips into the right branch. Thus an impulse descending from above would have to traverse a slightly longer route to reach the right branch than the left and might, therefore, inscribe an aberrant QRS complex whereas an idioventricular beat arising in the bundle below the level of greatest destruction might be expected to have a more direct path to the right branch and therefore not be delayed appreciably in its spread to the right side.

SUMMARY

Cases previously reported exhibiting rapid retrograde sequences in the presence of high-grade heart-block have furnished no evidence regarding the mechanism of these sequences. We report three cases with somewhat different forms of behavior, all of which yield data bearing on this problem.

In Case 1 the duration of retrograde sequences is shown to be influenced by their proximity to other retrograde sequences.

In Case 2 the retrograde sequences occur in the presence of 2-to-1 heart-block. The auriculoventricular intervals are unusually long and the retrograde sequences less prolonged. A much shorter retrograde interval is observed following a long rest period. This case appears to furnish an instance of reciprocal beating, the excitatory process traveling from auricles to ventricles and then back to auricles.

In Case 3 isolated forward and retrograde sequences were recorded in short strips of tracing. The forward sequences exceeded in duration the retrograde sequences by about 0.01 second. After forward conduction ceased, retrograde sequences were no longer observed.

The phenomena observed in these three cases may be accounted for by the hypothesis that retrograde sequences in high-grade heart-block are due to retrograde transmission of the excitatory process through the area of block; they cannot be satisfactorily explained on the basis of mechanical stimulation of auricles by ventricles.

It is suggested that the association of high-grade heart-block with normal transmission intervals is due to a short critical area for conduction in the bundle. More serial sections of junctional tissues in cases of so-called intermittent heart-block are required to establish or disprove this view.

The functional capacity of junctional fibers to conduct the excitatory process does not always bear a close relationship to the histological appearance. Thus it was found in Case 3 that a few greatly atrophied fibers in the right branch functioned without delay while a much larger group of normal-appearing fibers in the main bundle failed to function.

Aberrations in QRS complexes short of complete bundle-branch block are not necessarily due to lesions below the branching of the main bundle. They may be caused by lesions in the lower part of the main bundle located in such a position that the pathway to one of the main branches is longer than the other.

Sudden apparently spontaneous changes among normal rhythm, incomplete, and complete block occurred in our Case 3 independently of demonstrable vagus or sympathetic nerve effects.

Our thanks are due to Dr. Edward B. Krumbhaar, Dr. Herbert Fox, and Dr. John Eiman for their expert advice and assistance in the preparation and study of the serial sections.

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ELECTROCARDIOGRAPHIC CHANGES IN DIPHTHERIA

I. Complete Auriculoventricular Dissociation*

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THERE is probably no acute disease in which changes in the circulatory system and cardiac mechanism occur as suddenly as in diphtheria. Such changes are among the most serious complications of the disease, and their importance is increased because of the fact that the medical profession is practically helpless in its efforts to prevent their occurrence or to remedy them after they have become evident. Further study of these effects in their various phases, therefore, seems justified.

This paper deals with the electrocardiographic observations on nineteen diphtheritic patients who developed complete auriculoventricular dissociation. Two distinct types of complete auriculoventricular dissociation occurring in diphtheria are described. Delayed P-R conduction preceding the onset of complete block is demonstrated. The frequent occurrence and probable causes of delayed QRS interval are discussed, and the striking similarity between the electrocardiographic abnormalities occurring in diphtheria and as a result of the toxic effects of digitalis is emphasized.

Several excellent studies of electrocardiographic observations in diphtheria have appeared in recent years. McCulloch[1] in 1920 observed 18 abnormal electrocardiograms in 80 consecutive cases of diphtheria. These vary from inverted T-waves to ventricular tachycardia, intraventricular conduction defects, bundle-branch block, and complete auriculoventricular block.

Smith[2] studied electrocardiograms from 242 consecutive cases of diphtheria. Simple tachycardia was the only abnormality observed in 72 per cent of his cases. Of the remaining cases, 65 per cent had sinus arrhythmia or sino-auricular block during convalescence. Premature contractions were present in 20 per cent, while 15 per cent of the remaining cases, or a little over 4 per cent of the total series, developed a high grade heart-block about the seventh day of the disease. The block was practically always of sudden onset and was followed by death within forty-eight hours in three-fourths of the cases; none of the patients recovered. Smith observed no instance of low grade heart-block. It is interesting to note that one of his patients resumed a normal mechanism, with the exception of markedly inverted T-waves, after complete heart-block but died suddenly the next day.

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Marvin[3] in an extensive survey of past writings, discussed the clinical, pathological, and electrocardiographic aspects of the problem and included an analysis of 90 patients of his own. He concluded that the only electrocardiographic abnormality of value in estimating cardiac damage or impending death is faulty conduction, either auriculoventricular or intraventricular. His autopsied cases showed varying degrees of myocarditis, at times including inflammatory changes of the conduction system. He described one case, suspected clinically of myocardial involvement, in which normal electrocardiograms were frequently obtained but which at autopsy showed marked myocarditis. The conduction system, histologically, was quite normal.

Parkinson[4] reported one patient with complete heart-block occurring in diphtheria, who is known to have recovered. Block was demonstrated by polygraph on the twenty-third day of the illness. Auricular fibrillation was noted four days later and was still present when the patient was seen six months later.

At least two instances of partial heart-block in diphtheria have been reported. Hume[5] published a polygraphic tracing showing 2-1 heart-block, and Marvin and Buckley[6] mention a similar case described by Hecht in which 2-1 heart-block persisted for four months and was followed by recovery.

Before analyzing the results of this study, a statement of each case is presented, with description of the electrocardiograms, and a brief summary of the cases is given in Table I.

TABLE I

CASE NO.	SEX	AGE	ANTITOXIN UNITS	ADMINISTRATION DAY OF DISEASE	DAY OF DISEASE BLOCK WAS DISCOVERED	DURATION OF OBSERVATION OF BLOCK
1	F	15	20,000	4th day	10th day	4 days
			40,000	7th day		
2	M	5	40,000	6th day	7th day	Less than one day
3	F	8	40,000	3rd day	7th day	Less than one day
4	M	4	40,000	4th day	8th day	Less than one day
5	F	2	None		Unknown	4 days
6	F	5	40,000	4th day	8th day	Less than one day
7	F	5	20,000	2nd day	6th day	2 days
			20,000	6th day		
8	M	14	40,000	5th day	12th day	5 days
9	M	7	40,000	6th day	10th day	1 day
10	F	5	40,000	3rd day	8th day	4 days
11	M	5	Unknown	5th day	10th day	Less than one day
12	M	13	40,000	4th day	5th day	4 days
13	F	6	20,000	3rd day	11th day	Less than one day
			40,000	6th day		
14	M	7	10,000	2nd day	10th day	1 day
			10,000	4th day		
15	F	2	45,000	4th day	9th day	3 days
16	F	3	10,000	3rd day	7th day	4 days
			10,000	5th day		
17	M	9	40,000	7th day	9th day	1 day
18	F	18	40,000	5th day	7th day	10 days
19	M	10	Unknown	7th day	10th day	Less than one day
			40,000	10th day		

CASE REPORTS

CASE 1.—A white girl, 15 years old, received 20,000 units of antitoxin on the fourth day, and 40,000 units on the seventh day. The electrocardiogram of the seventh day shows a normal mechanism with a rate of 130, left ventricular preponderance and T-wave in the opposite direction to the main ventricular deflection in Leads II and III. A record taken on the tenth day shows complete heart-block,

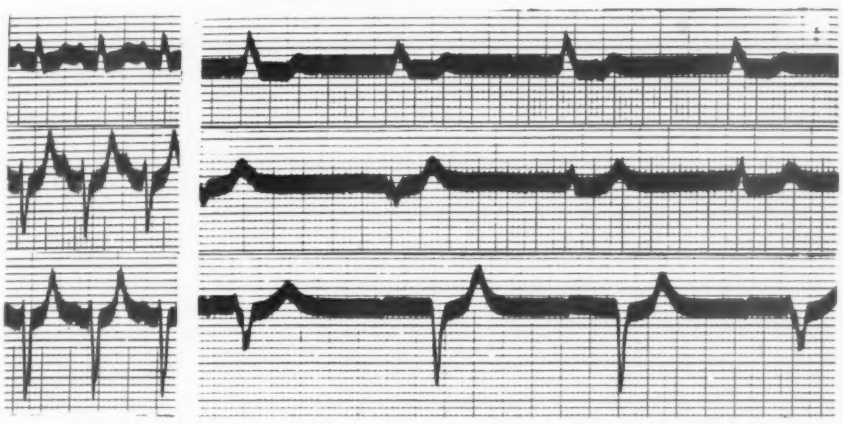

Fig. 1.—From Case 1. The first part is a record taken on the seventh day of disease showing normal mechanism, simple tachycardia of 130, and left ventricular preponderance. The T-waves in Leads II and III are opposite in direction to the main ventricular deflection. The second part was taken on the tenth day of disease and shows complete heart-block with an auricular rate of 80 and ventricular rate of 50, both slightly irregular. There is left ventricular preponderance, QRS interval of 0.12 second, variation of ventricular complexes and T-waves opposite in direction to main ventricular complexes in Lead III.

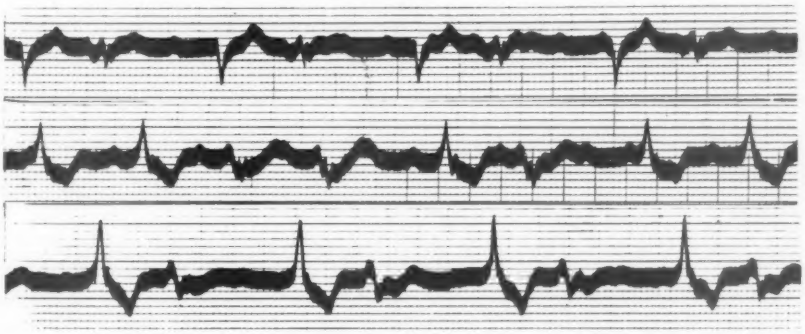

Fig. 2.—From Case 1, taken on the twelfth day of disease. Record shows complete heart-block with auricular rate of 200 and ventricular rate of about 90. There is coupled rhythm in Leads I and III, right ventricular preponderance and T-waves are in opposite direction to the main ventricular complexes.

QRS interval of 0.12 second, left ventricular preponderance, and variation in the ventricular complexes (Fig. 1). The auricular rate is 80 and the ventricular 50, both slightly irregular. On the twelfth day there is a definite coupled rhythm in Leads I and III, right ventricular preponderance, an auricular rate of 200, and a ventricular rate of 90, the latter slightly irregular because of the coupled rhythm (Fig. 2). Death occurred on the thirteenth day.

CASE 2.—A white boy, 5 years old, received 40,000 units of antitoxin on the sixth day. An electrocardiogram taken on the seventh day of the disease shows complete heart-block with a ventricular rate of 163 and an auricular rate of 155. The ventricular complexes are essentially normal except for a delay in the QRS interval

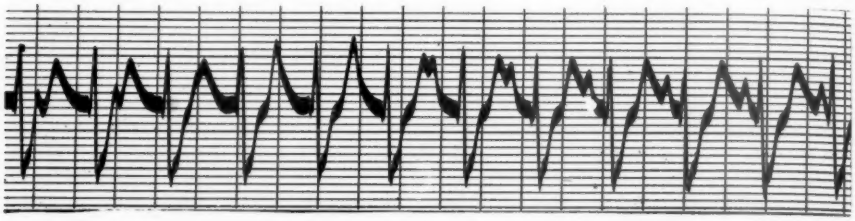

Fig. 3.—From Case 2. Lead II of a record taken on the seventh day of the disease showing complete heart-block with auricular rate of 155 and ventricular tachycardia of 163. There is right ventricular preponderance and delayed QRS interval of 0.12 second. P-waves are easily recognizable.

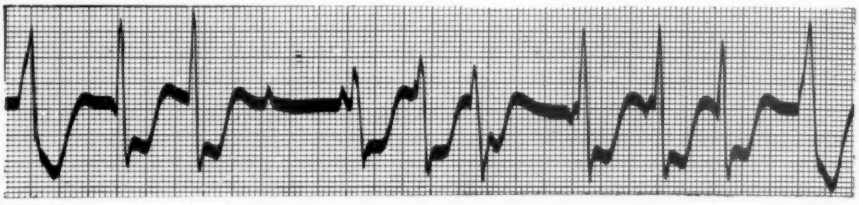

Fig. 4.—From Case 3. Lead II of a record taken on the seventh day showing complete heart-block. The auricular rhythm is fairly regular with a rate of 110. P-waves are prominent but frequently change their form. Ventricular rhythm is irregular with a rate of about 120. Complexes vary in Leads II and III, and there is right ventricular preponderance.

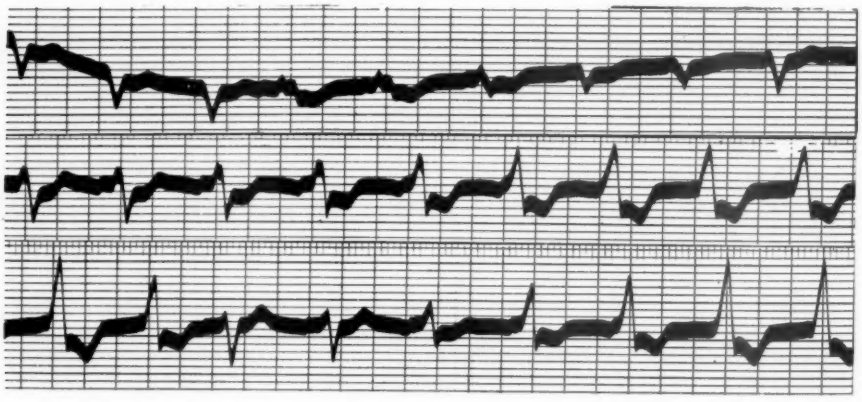

Fig. 5.—From Case 4. Record taken on the eighth day of the disease showing complete heart-block with auricular rate of 90 and ventricular rate of 100. The ventricular complexes vary gradually from positive to negative. QRS interval varies from 0.12 to 0.16 second, and T-wave is always in opposite direction to main ventricular deflection.

to 0.12 second. There is right ventricular preponderance, and T-waves are opposite the main ventricular deflection (Fig. 3). Death occurred shortly after this record was taken.

CASE 3.—A white girl, 8 years old, received 40,000 units of antitoxin on the third day of the disease. An electrocardiogram taken on the seventh day shows complete heart-block with cardiac action due entirely to short runs of ventricular tachycardia, varying from 3 to 11 beats. QRS interval varies from 0.1 to 0.12 second. The ventricular complexes vary in shape, and ventricular rhythm is irregular with a rate of 120. Definite P-waves are distinguishable, but nowhere do they seem to stimulate ventricular contraction. The P-waves change their form,

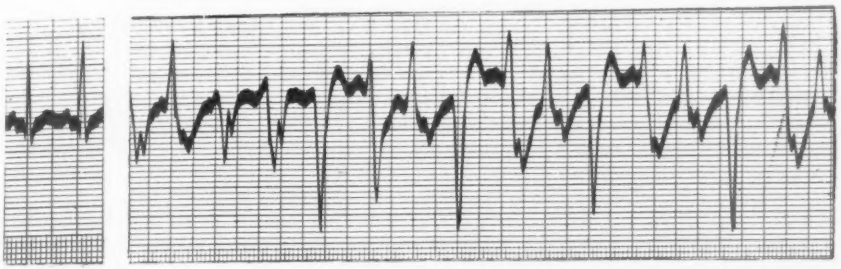

Fig. 6.—From Case 6. First record, taken on the eighth day of disease, shows normal mechanism, right ventricular preponderance, and simple tachycardia of 136. The second record, taken four hours later, shows rapid and irregular ventricular tachycardia with bizarre and rapidly changing ventricular complexes, which at times are alternating. QRS interval varies but at times is 0.2 second. P-waves are not recognizable.

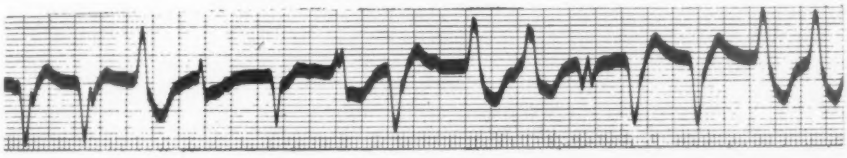

Fig. 7.—From Case 7. Record taken on the eighth day of disease shows an irregular ventricular tachycardia of about 130. The ventricular complexes vary in shape, at times alternate in direction and QRS interval is definitely prolonged.

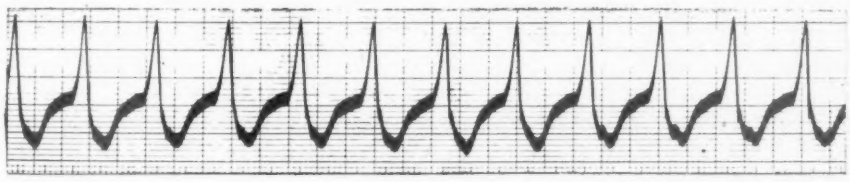

Fig. 8.—From Case 7, taken the day after Fig. 7. Record shows a regular ventricular tachycardia of 120, right ventricular preponderance, and delayed QRS interval of 0.16 second. Auricular rhythm is regular with a rate of 113.

and the auricular rhythm is fairly regular with a rate of 110 (Fig. 4). Death occurred on the seventh day.

CASE 4.—A white boy, 4 years old, received 40,000 units on the fourth day of the disease. An electrocardiogram taken on the eighth day shows complete block with a fairly regular ventricular rate of about 120. The auricular rate cannot be distinguished. A record of the following day shows the same block and also intraventricular block, with complexes gradually varying from positive to negative in all leads. QRS interval is prolonged, being from 0.12 to 0.16 seconds. The ventricular rate is 100, and auricular rate 90, both regular (Fig. 5). The patient died the same day.

CASE 5.—A white girl, 2 years old. The date of onset is not definitely known but was about three weeks before entry. The patient developed paralysis of the palate one week before entry. A record taken four days after entry shows complete heart-block, ventricular rate of 140, auricular rate 100, both regular. Ventricular complexes are normal except for low voltage. Death occurred five days after admission to the hospital.

CASE 6.—A white girl, 4 years old, received 40,000 units of antitoxin on the fifth day of the disease. An electrocardiogram taken on the eighth day is normal except for a tachycardia of 136. A record four hours later shows rapid and irregular ventricular tachycardia of 140 with rapidly changing ventricular complexes, which at times are alternating. P-waves are not distinguishable. QRS interval varies but is markedly prolonged to 0.2 seconds (Fig. 6). Death occurred within an hour of this record.

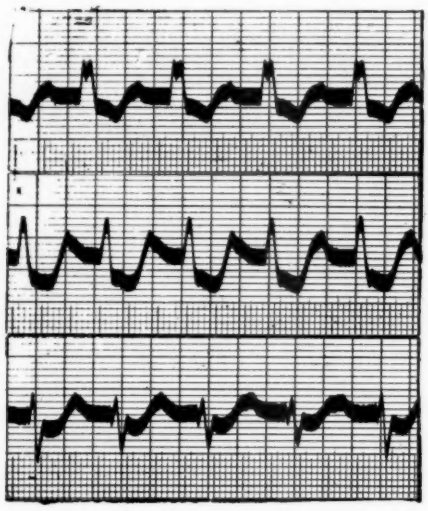

Fig. 9.

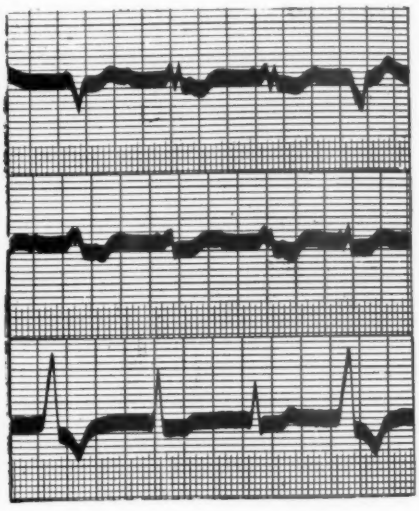

Fig. 10.

Fig. 9.—From Case 9. Record, taken on the seventh day of the disease, shows tachycardia of 100, delayed P-R conduction of 0.22 second, prolonged QRS interval of 0.12 second and T-waves in opposite direction to main ventricular deflection.

Fig. 10.—From Case 9. Record taken on the tenth day shows complete heart-block, with auricular rate of 140 and ventricular rate about 90. There is right ventricular preponderance, the ventricular complexes vary markedly and QRS interval is prolonged. In Lead III. T-waves vary from upright to downward in spite of the fact that the ventricular complexes are all upright.

CASE 7.—A white girl, 5 years old, received 20,000 units of antitoxin on the second day of the disease and also on the sixth day of the disease. An electrocardiogram taken on the seventh day shows ventricular tachycardia and complete heart-block, with impulses arising regularly in the right ventricle. The auricular rate is 150 and the ventricular rate 120. A record on the following day shows an irregular ventricular tachycardia of 130, with rapidly changing, bizarre ventricular complexes. The auricular rate is 110 (Fig. 7). On the ninth day, the day of death, the heart again became regular, and the tracing resembles closely the one taken two days before. The auricular rate is 113 and the ventricular rate 120 (Fig. 8). QRS interval varies but is definitely prolonged to 0.16 second.

CASE 8.—A white boy, 14 years old, received 40,000 units of antitoxin on the fifth day of the disease. An electrocardiogram taken on the twelfth day shows complete dissociation and an irregular mechanism interpreted as a ventricular tachycardia. The auricular rate is 100 and the ventricular 120. Two days later an essentially similar record was obtained in which the ventricular rate is 140; the auricular rate cannot be distinguished. QRS interval in both records is definitely prolonged. Death occurred on the seventeenth day.

CASE 9.—A white boy, 7 years old, received 40,000 units of antitoxin on the sixth day of the disease. An electrocardiogram taken on the seventh day shows a normal mechanism with delayed P-R conduction of 0.22 second. The QRS interval is about 0.12 second, the R-wave is splintered in Lead I, and the T-wave is opposite in direction to the QRS in all leads (Fig. 9). A record taken on the tenth day shows complete dissociation with a regular auricular rate of 140 and an irregular ventricular rate of 90. Ventricular complexes vary markedly, QRS interval is prolonged, and in Lead III the T-wave at times is inverted and at times

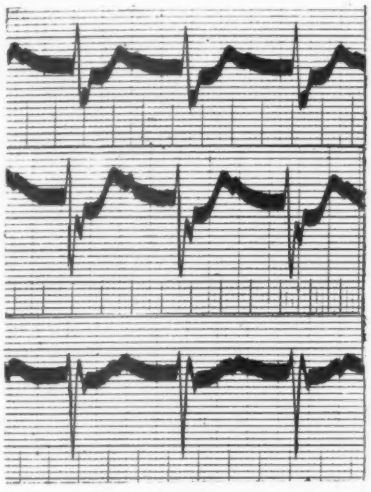

Fig. 11.

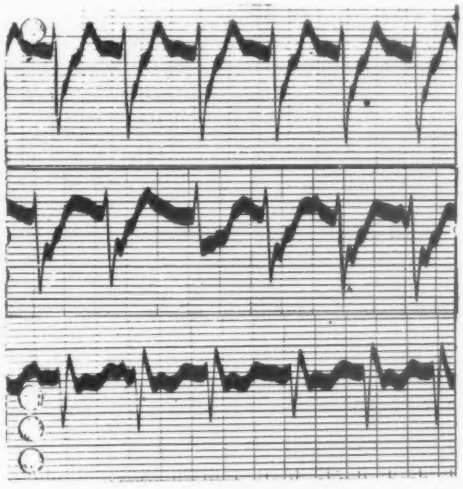

Fig. 12.

Fig. 11.—From Case 10. Record taken on the eighth day shows delayed P-R conduction of 0.36 second. There is marked left ventricular preponderance and prolonged QRS interval. The rhythm is regular and rate 80.

Fig. 12.—From Case 10. Record taken the day after Fig. 11 shows complete heart-block with auricular rate of 110 and ventricular rate of 120, the latter being somewhat irregular. QRS interval is 0.12 second.

upright, in spite of the fact that the QRS complexes are all upright (Fig. 10). Death occurred the following day.

CASE 10.—A white girl, 5 years old, received 40,000 units of antitoxin on the third day. Electrocardiograms taken on the seventh and eighth days of the disease show nodal rhythms and rather bizarre complexes and rates of 110 and 100 respectively. A record taken six hours later shows ventricular complexes which are essentially unchanged, but P-waves are distinguishable, the P-R interval is 0.36 second, and the rate has dropped to 80. The S-wave is splintered in Lead II, and T-waves are in opposite direction to the main ventricular deflection (Fig. 11). In a record of the following morning there is complete dissociation with an auricular rate of 110 and a ventricular rate of 120, both regular. The third complex in Lead II differs from the others (Fig. 12). QRS interval is 0.12 second in both of these records. Death occurred on the eleventh day.

CASE 11.—A white boy, 5 years old, received antitoxin on the fifth day, but the amount is unknown. He entered the hospital on the tenth day with a diagnosis of dilatation of the heart and died several hours after admission. The electrocardiogram shows a fairly regular ventricular rhythm with rate of about 60. P-waves are small but at times indistinguishable so that the auricular rate cannot be determined. There is marked widening of the QRS interval to almost 0.2 second. The ventricular complexes vary markedly in height in Lead III, and the T-waves are opposite in direction to the main ventricular deflection in all leads.

CASE 12.—A white boy, 13 years old, received 40,000 units of antitoxin on the third day of the disease. On the fifth day the pulse rate dropped to 65. An electrocardiogram taken at this time shows complete heart-block, low voltage, slight delay in QRS interval of 0.1 second, an auricular rate of 118, and ventricular rate of 66, both regular. Death occurred on the eighth day.

CASE 13.—A white girl, 6 years old, received 20,000 units of antitoxin on the third day of the disease and 40,000 units on the sixth day. An electrocardiogram

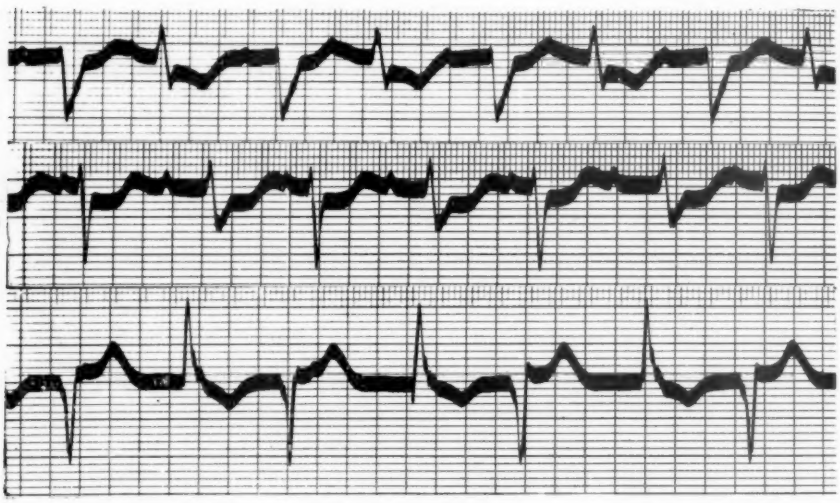

Fig. 13.—From Case 18. Record shows complete heart-block and alternating bidirectional ventricular rhythm. The auricular and ventricular rates are about 80, but the P-R interval varies markedly. QRS interval is prolonged to 0.16 second at times. T-waves are in the opposite direction to main ventricular deflections.

taken on the day of death, which was the eleventh day of the disease, shows complete heart-block with a slightly irregular ventricular rate of 160. P-waves are distinguishable but occur rather irregularly. QRS interval is about 0.1 second.

CASE 14.—A white boy, 7 years old, received 10,000 units of antitoxin on the second and fourth days of the disease. An electrocardiogram taken on the tenth day of the disease shows complete heart-block with slightly irregular ventricular rate of 126 and an auricular rate of 100. Ventricular complexes vary slightly but are essentially normal except for QRS interval of 0.12 second. Death occurred the following day.

CASE 15.—A white girl, 2 years old, received 45,000 units of antitoxin on the fourth day of the disease. The pulse rate varied from 100 to 140 until the ninth day when it fell to 50. An electrocardiogram taken on the tenth day shows complete heart-block with an auricular rate of 100 and a ventricular rate of 40,

both regular. There is left ventricular preponderance, and QRS interval varies from 0.12 to 0.16 second. A record of the eleventh day shows the same. Death occurred on the twelfth day.

CASE 16.—A white girl, 3 years old, received 10,000 units of antitoxin on the third and fifth days. An electrocardiogram taken on the seventh day shows complete heart-block, marked variation in the ventricular complexes, ventricular rate of 110 somewhat irregular, and an auricular rate which could not be determined. Another record taken two days later shows complete heart-block with fairly normal ventricular complexes except for low voltage, a ventricular rate of 97 and auricular rate of 136, both regular. Death occurred on the eleventh day.

CASE 17.—A white boy, 9 years old, received 40,000 units on the seventh day of the disease. An electrocardiogram taken on the ninth day shows complete auriculoventricular dissociation, delayed intraventricular conduction of from 0.12 to 0.17 second, inverted T-waves, regular rhythm, ventricular rate of 90, and an auricular rate of 126. QRS complexes are upright in all leads. Death occurred on the tenth day.

CASE 18.—A white girl, 18 years old, received 40,000 units of antitoxin on the fifth day of the disease. On the seventh day the pulse fell to 60, and a record showing complete heart-block was obtained. From this day until death, on the seventeenth day, sixteen tracings were made. All show complete auriculoventricular dissociation varying from regular to irregular and in rate from 60 to 140. There is marked variation in ventricular complexes and in QRS intervals up to 0.16 second. Alternating bi-directional ventricular rhythm is seen twice (Fig. 13).

CASE 19.—A white boy, 10 years old, received two doses of antitoxin from the seventh to the tenth day of the disease, at which time he entered the hospital and was given 40,000 units in addition. On entrance the patient was pale and pulseless; heart was dilated and irregular. An electrocardiogram shows complete auriculoventricular dissociation with irregular rhythm and varying ventricular complexes, also marked delay in QRS conduction up to 0.2 second. Death occurred four hours after entry.

DISCUSSION

This study is based upon observations of all cases of clinical diphtheria in which the presence of complete heart-block was proved electrocardiographically. In no instance was resumption of a normal rhythm observed following the institution of block. These patients were all under twenty years old, and in every instance death occurred in from a few hours to ten days following the appearance of complete heart-block. All except one received substantial doses of diphtheria antitoxin, some as early as the second, third and fourth days of the disease. The duration of the disease before the observation of block varied from six to twelve days. In one case this period was unknown.

There are at least two ways in which complete auriculoventricular dissociation may occur. One is disfunction of the A-V bundle itself, manifested first as a delayed P-R interval, then presumably by a period of dropped beats, and finally a complete block with an independent but slow ventricular rhythm. This may be the result of an actual organic involvement of the conduction system.[3] The other way is by a func-

tional disarrangement, probably caused by toxins, without irreparable damage to the conduction system, as evidenced by the case reported by Smith,[2] in which a normal rhythm returned after complete heart-block. This would indicate that anatomical destruction of the conduction system is not necessary for the production of block. Chloroform and digitalis poisoning and asphyxia cause other toxic states which may be associated with heart-block, but in which recovery is not uncommon.

Complete auriculoventricular dissociation also occurs as a result of increased irritability of the ventricular muscle from various poisons which set up an independent rhythm in the ventricles, i.e., a ventricular tachycardia with a rate faster than that of the sinus or the auricles. Under these conditions dropped beats are not to be expected. This augmented irritability is often associated with defective intraventricular conduction, shown by prolonged QRS interval and rapidly changing

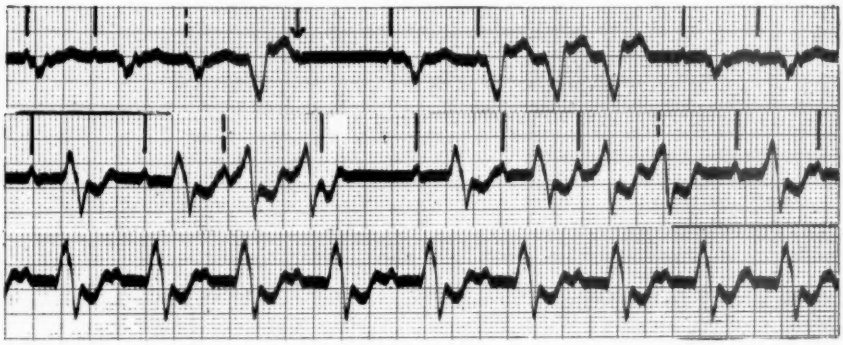

Fig. 14.—Record from a case not included in this series because complete heart-block was not observed. The solid lines point to definite P-waves, the broken lines to probable P-waves and the arrow in Lead I to a dropped beat. P-R interval is 0.26 second when it is recognized, ventricualr escape is common, the ventricular rhythm is irregular, and QRS interval is 0.18 second. The auricular rhythm is very irregular and at times seems to disappear for short periods.

form of ventricular complexes from beat to beat. White[7] described two methods by which the ventricular rate exceeded the auricular rate. One occurs when the automatic stimulus production in the atrioventricular node is released by any factor which depresses and slows the sino-auricular node; the other, which he characterizes as a rare type, occurs when the atrioventricular node becomes so irritable as to escape from control of the sino-auricular node. He described three cases of his own and several from the literature, three of which were apparently due to digitalis and one to strophanthus. After large doses of atropine Wilson[8] saw this phenomenon during forced respiration. Christian[9] reported four cases showing varying degrees of block and rapidly changing form of ventricular complexes which he attributed to digitalis administration. Hewlett and Barringer[10] point out that digitalis first decreases the heart rate but later causes independent auricular and

ventricular rhythms. Under these circumstances the ventricular rate approaches or exceeds the auricular rate. They report a clinical case of this kind in which the patient died twenty-four hours after onset. Heard and Colwell[11] cite a case of permanent block of the right bundle-branch with transient periods of complete auriculoventricular dissociation which were definitely related to digitalis administration. In most of these periods the ventricular rate exceeds the auricular rate.

It seems surprising that minor grades of heart-block are not more frequently encountered in diphtheria. From observations of cases on which many electrocardiograms were made, it is evident that profound changes in cardiac function occur very rapidly. Three records, however, are shown in which the P-R interval is definitely abnormal. In Case 9 (Fig. 9) the P-R interval is prolonged to 0.22 second with a regular rhythm and a rate of 100. Three days later there is complete block with an auricular rate of 130 and ventricular rate of 90 (Fig. 10). In Case 10 (Fig. 11) P-waves are definite and P-R interval is

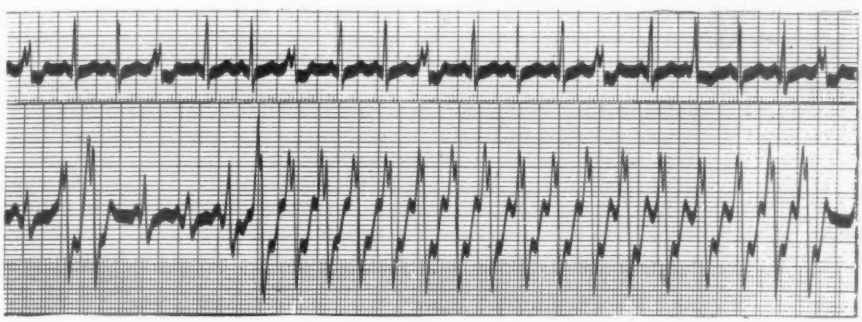

Fig. 15.—Record from a case not included in this series. Lead I shows normal mechanism except for frequent extrasystoles. Lead III shows extrasystoles and one short run of ventricular tachycardia with rate of 180. The patient made an uneventful recovery.

markedly prolonged to 0.36 second with a regular rhythm and rate of 80. On the following day there is complete block with an auricular rate of 110 and a ventricular rate of 120 (Fig. 12). The third record is from a case not included in this series because complete heart-block is not demonstrated (Fig. 14). Ventricular complexes are bizarre in shape; QRS interval is markedly prolonged to 0.18 second. Ventricular escape is common in Leads I and II; but where ventricular complexes follow P-waves, the P-R interval is 0.26 second. The wave marked in Lead I represents a dropped beat. Both auricular and ventricular rhythms are irregular.

Ventricular tachycardia in diphtheria may be a transient disorder and is not necessarily fatal. For example, Fig. 15 is a record taken from a patient not included in this series, but who showed this transient disorder from which he promptly recovered. In this record ventricular extrasystoles are common, and a few runs of ventricular

tachycardia occur; but conduction is not seriously impaired because normal conduction sequence prevails. It is interesting to compare this with Fig. 4 in which only short runs of extrasystoles are seen. In this figure there are several pauses as long as one second containing well-marked P-waves but normal ventricular complexes do not follow. Auriculoventricular conduction does not occur.

The individual records of ventricular tachycardia in this series show marked degrees of variation in rhythm. Some are quite regular, as described in Cases 2, 5, 7, 8, 10, 12, 15 and 17 (Figs. 4 and 8); some show a gradual but rhythmical change as in Case 4 (Fig. 5); while still others show rapidly changing and wildly bizarre complexes, as in Cases 6 and 7 (Figs. 6 and 7), and to a slighter extent in Case 9 (Fig. 9).

Alternating bi-directional ventricular tachycardia can be found in Cases 6 and 7 (Figs. 6 and 7), lasting only during several beats. Case 18 (Fig. 13), however, exhibits a ventricular rhythm with alternating complexes in opposite directions for a considerable period. This phenomenon is observed in two records taken six hours apart, after which it changes to a regular ventricular rhythm arising in the right ventricle. Alternating bi-directional ventricular rhythm was first described by Schwensen.[12] Palmer and White[13] reviewed the literature in 1928, finding only thirteen cases illustrating this phenomenon. Six months later Marvin[14] reported five additional examples. All of these were cases of middle-aged patients with damaged and fatigued myocardia, who had received substantial or excessive doses of digitalis. The authors believe that this drug constituted the most striking etiological factor. This represents a serious cardiac condition, as death usually occurred in several days.

Prolongation of the QRS interval is one of the most constant changes of the ventricular complexes in this series. In fourteen cases it varied from 0.12 to 0.2 second. In two cases it was 0.1 second, the upper limit of normal; while in only two cases (Cases 5 and 16) was it under 0.1 second. Prolongation of the QRS complex has been attributed in part to dilatation of the heart with resultant lengthening of the conduction paths. While this may contribute, it seems inconceivable that the paths of conduction can be increased to two and three times their normal length. It appears more likely that toxic depression in diphtheria impairs conduction. That this actually occurs is shown in the following article of this series by demonstrating electrocardiographic tracings of patients with marked QRS prolongation and even bundle-branch block followed shortly by clinical and electrocardiographic recovery. Wilson and Herrmann[15] reported a case of uremia in which the QRS interval increased to 0.2 second on the day of death. They attributed this to a toxic depression of the conductivity of the Purkinje system. In his studies of the toxic rhythms due to digitalis, Luten[16] states that digitalis is known to depress intraventricular conduction.

In another article[17] he says, "Our patients who exhibited signs of severe toxemia and at the same time showed independent ventricular rhythm gave records which contained also evidence of impaired intraventricular conduction." Robinson,[18] on the other hand, reports cases in which prolongation of the QRS interval was decreased when clinical improvement occurred as a result of rest and digitalis.

Though none of the patients of this series received digitalis medication of any sort during their stay in the hospital, the electrocardiographic changes show a striking similarity to some of the toxic effects of digitalis. Of the evidences of toxicity, prolonged P-R coduction has been pointed out in Cases 9 and 10 (Figs. 9 and 10). Complete heart-block with slow ventricular rhythm occurred in Cases 1, 11, 12, and 15 (Fig. 1). A striking coupled rhythm quite similar to that seen as a digitalis effect is shown in Case 1 (Fig. 2). Of the less frequently seen but well-known disorders following digitalis are ventricular tachycardia with a ventricular rate faster than the auricular rate in Cases 2, 5, 7, 8, and 10 (Figs. 3, 8, and 12), irregular ventricular tachycardia in Cases 3, 4, 7, 9, 12, 13, 14, 16, and 18 (Figs. 4, 6, and 7), varying and bizarre ventricular complexes in Cases 1, 3, 4, 6, 7, 9, 16, 18, and 19 (Figs. 1, 5, 6, 7, and 10), delayed QRS conduction in Cases 1, 3, 4, 6, 7, 8, 9, 10, 11, 14, 15, 16, 17, 18, and 19 (Figs. 1, 2, 4, 5, 6, 7, 8, 9, 10, 12, and 13), and alternating bi-directional ventricular tachycardia in Cases 6, 7, 18, and 19 (Figs. 6, 7, and 13). This supports the experience of pediatricians that digitalis is definitely contraindicated in diphtheria.

SUMMARY

1. Nineteen cases of complete heart-block occurring in diphtheria were studied electrocardiographically. All terminated fatally.

2. Heart-block in diphtheria probably results from a toxic action upon the conduction system which renders it functionally inactive or from an irritation of the ventricular muscle which results in the setting up of an independent ventricular rhythm with a rate faster than that of the auricles. Both effects may occur simultaneously.

3. Some of the effects of diphtheria on the cardiac mechanism simulate closely the toxic effects of digitalis.

4. The opinion that digitalis is contraindicated in diphtheria is substantiated.

The author wishes to express his appreciation to Dr. J. A. Toomey and the Department of Contagious Diseases for permission to study these cases.

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VENTRICULAR FIBRILLATION: ITS RELATION TO HEART-BLOCK

Report of a Case in Which Syncopal Attacks and Death Occurred in the Course of Quinidine Therapy*

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PERSISTENT ventricular fibrillation in man is incompatible with life. With its onset there is unconsciousness, and when it continues for more than a few minutes, death ensues. This occurs because the cardiac output falls to a level far below that necessary to maintain an adequate circulation. Clinically, then, ventricular fibrillation is manifested by syncope or sudden death. How frequently ventricular fibrillation is responsible for syncope is unknown. It is significant, however, that in the few instances in which electrocardiographic studies have been made during attacks of unconsciousness, flutter or fibrillation of the ventricles has been revealed in several. It is further significant that but few instances of heart-block and ventricular standstill are on record. This has been regarded as the common mechanism of syncope and sudden death in the Morgagni-Adams-Stokes syndrome. Lewis believes that ventricular fibrillation is probably the chief cause of fatal syncope.

This abnormal rhythm is, then, of importance to the clinician. His immediate problems are: (1) under what conditions does it occur; (2) what are its precursory mechanisms, and (3) how is it influenced by drugs. The purpose of the present communication is to discuss these problems and to report an additional case† of ventricular fibrillation or flutter-fibrillation proved by electrocardiogram.

The characteristic features of fibrillation of the ventricles in man were reviewed by Lewis in the third edition of his *Mechanism and Graphic Registration of the Heart Beat*. Since the publication of this edition several other likely cases have been reported by Reid,[2] Haines and Willius,[3] Levine and Mattin,[4] Donath and Kauf,[5] von Hoesslin,[6] Gallavardin and Berard,[7] and De Boer.[15] The case which we report showed electrocardiographic abnormalities consistent with those previously accepted as criteria for circus movements of greater or less regularity occurring in the ventricles and corresponding to curves recorded from experimental animals in whom ventricular fibrillation was seen.

*From the First Medical Service of the Boston City Hospital.

†The case here described was outlined by Sidel and Dorwart[1] in their article *Quinidin Sulphate in Auricular Fibrillation*, but the electrocardiographic aspects were not fully considered.

The unusual feature presented by this case was the occurrence of syncopal attacks associated with the ventricular acceleration. These attacks were repeated many times during the last eight hours of the patient's life, and the cardiac mechanism is explained by electrocardiographic tracings taken during the attacks and in the intervening periods of consciousness.

CASE REPORT

V. L., a single woman of forty-eight years, was admitted to the Boston City Hospital January 19, 1926, complaining of shortness of breath of six months' duration. In July, 1925, she was confined to bed with an attack of dyspnea and orthopnea. Recovery was followed by moderate dyspnea on exertion, and on three subsequent occasions she had attacks of progressively severe dyspnea, orthopnea, and palpitation. The last attack began the latter part of December, 1925, since which time she had been confined to bed.

At the age of eleven she had her first attack of rheumatic fever. All joints were swollen, painful, and very tender. Following this she had attacks of rheumatic fever about every three years up to 1921.

From June 2, 1924, to June 18, 1924, she was a patient at the Boston City Hospital, her chief complaint at the time being shortness of breath and sore throat of ten days' duration. Her condition was diagnosed acute bronchitis. It was noted that for three years preceding this illness she had slight dyspnea on exertion. Examination on this admission showed a regular cardiac action except for occasional extrasystoles. There was some enlargement of the heart to the left as determined clinically and by x-ray examination. No other essentials were noted.

When admitted January 19, 1926, the patient was found to be a well-developed and well-nourished, middle-aged woman in moderate respiratory distress. Breathing was rapid and labored, and orthopnea marked. There was cough at intervals of a few minutes. Except for slight redness of the right side of the faucial ring the examination of the head and neck was negative. The chest was barrel-shaped expansion on both sides being moderate and equal. The heart was definitely enlarged to the left, the apex impulse being in the anterior axillary line 13 cm. to the left of the midsternum. At the apex a thrill, probably diastolic in time, was felt. The apex rate was 140, absolutely irregular in force and rhythm. The first sound at the apex was loud and booming, the second sound weak. Loud to-and-fro murmurs were present, but timing was difficult because of the rapid rate. The radial pulse rate was 80, the pulse deficit 60. The lungs were resonant throughout, and the breath and voice sounds were normal. At both bases posteriorly, from the midscapula down, there were numerous coarse râles most marked on the left. The liver was palpable three fingerbreadths below the costal margin in the midclavicular line. Spleen and kidneys were not felt, and there was no evidence of fluid in the abdomen. Slight pitting edema was present over both legs. The radial arteries were soft.

Blood pressure: systolic 140 mm. mercury, diastolic 90 mm. White blood cell count 8,000. Urine: no albumin, no sugar, normal sediment, specific gravity of 1.016. Blood Wassermann reaction negative.

Absolute rest, repeated doses of ¼ grain of morphine, to be given subcutaneously, and large doses of the tincture of digitalis were ordered. The patient did not do well, and because of her frequent vomiting the nursing staff did not push the digitalis to the desired extent. On January 23, 1926, digitora pills, grains ii, three times a day were prescribed.

The apex beat on January 23 was recorded at 120-140, with a pulse deficit ranging from 25 to 40. There was slight general improvement, but the patient was still orthopneic, and there were many râles at both bases. The edema of the legs had disappeared. A poor prognosis was given.

The dose of digitora was changed to grains i, three times a day, on January 24, because of nausea and vomiting.

The electrocardiogram of January 26 demonstrated auricular fibrillation and frequent ectopic ventricular beats. The ventricular rate was 90-103.

Impovement was noted on January 28, while on digitora, grains i, three times a day, the apical rate being 90-100 with a pulse deficit of from 5 to 15. The patient looked better and was comfortable in bed. There was very little dyspnea, and no râles were heard at the bases.

On January 30 digitalis was discontinued and quinidine therapy instituted. After a total of 61 grains (4 gm.) in three days the quinidine was discontinued because of the marked nausea and gastric irritability it evoked. For several days following, nausea and vomiting persisted and little food was taken.

Digitora, grains ii, three times a day, was again ordered on February 5, and discontinued February 8. During this period no drop in pulse deficit was obtained, the drug being stopped because of nausea and vomiting. On the eighth she was allowed up in a chair for a half hour daily, not because of any improvement, but merely to secure a better state of mind.

On the ninth it was decided to give quinidine another trial, and accordingly a total of 123 grains (8.2 gm.) was given by the thirteenth. This therapy was interrupted after an initial dose of 3 grains because of nausea and vomiting. Nevertheless it was continued the following day, although nausea was still present. The patient was up in a chair for short periods. Orthopnea, dyspnea on exertion, and râles at both bases were present. She continued to do poorly and died February 13, after eight hours of recurrent syncopal attacks.

POST-MORTEM EXAMINATION

February 14, 1926. Twelve hours post-mortem. Body length 158 cm.

Peritoneal Cavity.—Numerous fibrous adhesions between gall bladder and omentum and pelvis, between large and small intestines, uterus, left ovary and tube; liver was 7 cm. below xiphoid and 2 cm. below costal margin. No excess of fluid.

Pleural Cavity.—No excess of fluid. A few firm fibrous adhesions in the upper right pleural cavity.

Pericardial Cavity.—Patches of firm, fibrous adhesions were found between visceral and parietal surfaces in the region of the left ventricle and both auricles and about the large vessels. Elsewhere the surfaces were smooth and shining. No excess of fluid.

Heart.—Weight 475 gm. The heart was large, firm, and with a much dilated left auricle. On section the myocardium showed no evidence of fibrosis. The inner surface of the left auricle was firm, smooth, and pinkish gray-white. The mitral valve was much thickened and contracted. There was a point on the margin of the valve that was bright red, irregular, and about 2 mm. in diameter. This did not arise above the surrounding surface. The chordae tendineae were shortened, thickened, and grayish white in appearance. Fibrous tissue had replaced some of the tissue of the papillary muscles, making them grayish red, firm, and short. The myocardium between the mitral and aortic valves was denser, firmer, and grayer than normal. Multiple section elsewhere revealed no gross fibrosis.

Measurements:	tricuspid valve	12.0 cm.	Circumference.
	pulmonary valve	8.2 cm.	
	mitral valve	8.5 cm.	
	aortic valve	6.5 cm.	
	left ventricle	1.3 cm.	Wall thickness.
	right ventricle	0.5 cm.	

Lungs.—The whole right lung was red, fairly firm, but crepitant throughout. The left lower lobe was firm, red, but crepitant. On section these portions were red, wet, and oozed considerable amounts of blood.

Spleen.—Weight 255 gm. It was large, soft and grayish purple. On section the organ was soft, very dark purplish red, and much pulp could be scraped away.

Liver.—Weight 1620 gm. It was regular, smooth, firm, and brownish red with markedly rounded edges. On section the organ was firm, purplish brown, and lobulations were visible. Gall bladder and bile ducts were negative.

Aorta.—A few irregular yellowish areas were found on the abdominal aorta. Otherwise it was negative.

Brain.—Weight 1315 gm. The surface was firm and pinkish gray. Multiple sections revealed no pathological changes.

Anatomical Diagnosis.—Chronic auricular endocarditis, chronic endocarditis of mitral valve with mitral stenosis, congestion and edema of lungs, acute splenic tumor, old pericarditis, congestion of liver and spleen, old pleuritis, old peritonitis, multiple leiomyoma of uterus, simple cysts of ovary, mucous polyp of cervix, arteriosclerosis.

DISCUSSION OF SYNCOPAL ATTACKS

On February 13, 1926, at 4 P.M., three hours after the last dose of 15 grains (1 gm.) of quinidine, the patient developed an unusual combination of symptoms which were repeated in cycles and which ended in death eight hours later.

The following note was made by the house officer: "About 4 P.M. I was called to see the patient and found her lying propped up in bed breathing stertorously. This breathing quieted down and finally stopped completely. She became yellow and cyanotic; the muscles of the left arm and both forearms twitched. The apex beat could not be detected, but after a minute the heart began to come back. During all this time the patient was unconscious, but now with the return of the heartbeat the patient began to regain consciousness. About fifteen minutes later she went through the following cycle: the heart rate at the apex becomes slower and slower and finally stops completely. With this the patient swoons, losing consciousness. She becomes pale and yellow, and then takes on a peculiar deathlike tint. The respiration becomes deeper, then stertorous, and finally stops. Ten or fifteen seconds later twitching of the muscles of the face and left arm occurs. Then after the heart has been stopped (apparently) for two minutes and ten seconds, it gradually begins to beat again. The patient's color begins to return. The apex beat, at first absolutely irregular for about

forty beats, becomes more rapid and coupled. In this coupled state it remains until a second attack. At moments the apex beat appears irregular, simulating fibrillation. Atropine, caffein, and adrenalin have been of no influence on these recurring attacks."

The patient's breathing just after the apparent loss of the apex beat was of the character of Cheyne-Stokes respiration. The breathing became deeper, and more and more stertorous, gradually reached a summit and gradually declined. The active period comprised on the average about 30 respirations. Each respiratory phase was relatively short

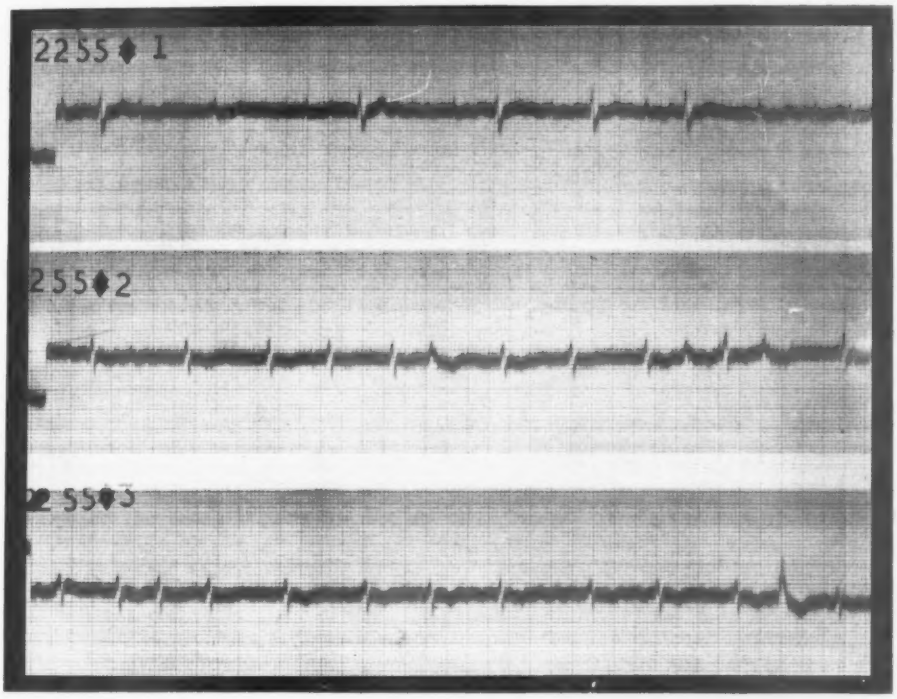

Fig. 1.—Electrocardiogram, Leads I, II, and III, January 26, 1926. Auricular fibrillation, ventricular rate 90-100, low voltage of ventricular complexes in all leads (amplitude not over 5 mm.), several ectopic ventricular contractions, especially in Lead I where alternate beats are abnormal for four couples following the fifth beat.

NOTE: In all figures scale on the ordinate in 10^{-4} volt, and on the abscissa is 0.04 second.

compared to the interval between. With the onset of the apneic period the patient was usually cyanotic and appeared dying. From ten to thirty seconds after this onset irregular beating at the apex could be detected and shortly after this the patient began to breathe slowly. Her color returned, and she gradually regained consciousness. With eyes wide open she gently moved her head on the pillow, slowly repeating that she could not live, that she was dying. These periods of consciousness lasted but a few minutes, and then the same cycle ap-

peared all over again. Thus for eight hours the patient vacillated from "death" to life about once every five or ten minutes.

When seen by one of us about three hours before death, the cyclic attacks were being frequently repeated. It appeard, however, that an

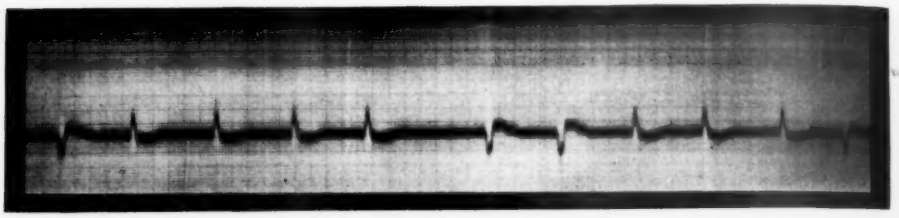

Fig. 2.—Electrocardiogram, February 13, 1926. Probable auricular fibrillation, ventricular rate 50-60, inverted T-waves, five complexes in opposite phase to the usual QRST deflections. NOTE: In this and the following illustrations the lead is either I or II, as a confusion arose in the original marking.

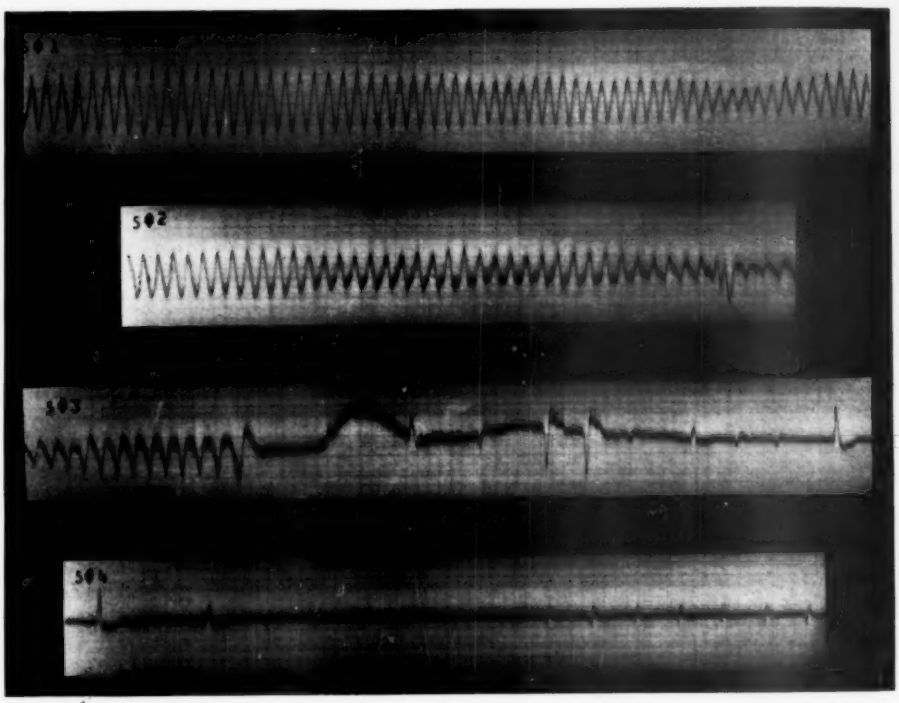

Fig. 3.—February 13, 1926. Record of an almost complete attack of ventricular tachycardia (see text). Recorded duration 32.8 seconds.

attack was initiated by the onset of a very rapid heart rate. The heartbeats were inaudible at the apex, but a trembling of the precordium could be felt during the time that this rate persisted, followed by the return of faint irregular beating of the heart at a much slower rate and finally the resumption of a relatively regular rhythm.

Electrocardiographic studies were made at this time. Technical difficulties and the long distance between the patient and the laboratory, with consequent telephone and hand signal relays, made accurate correlation between clinical and electrocardiographic records difficult. The electrocardiograms, however, are sufficiently clear to explain the mechanism of the attacks.

Fig. 1 is the electrocardiogram of January 26, 1926, eighteen days before the onset of the attacks preceding her death. It shows auricu-

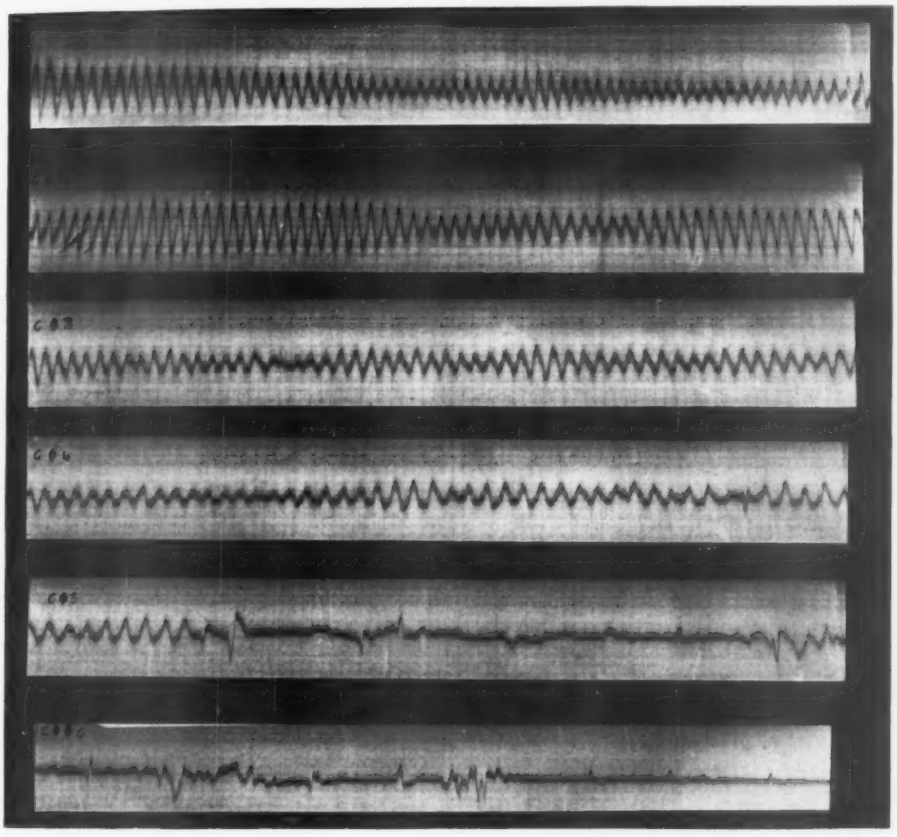

Fig. 4.—February 13, 1926. Record of another attack of tachycardia. Rate 220, slowing to 150 before the offset. Recorded length of paroxysm is about 71.6 seconds. Note temporary recovery of normal conduction in one beat near the end of strip 4.

lar fibrillation, rate 90-100, low T-waves in all leads, low voltage of QRS complexes (amplitude not over 5 mm. in any lead), and several ectopic ventricular contractions.

Fig. 2 is the record taken when the patient was seen by us February 13, 1926, and shows the type of rhythm existing between attacks of tachycardia. Absolute ventricular arrhythmia is present but with less evidence of auricular activity than in the previous tracing. The more

aberrant ventricular complexes are inverted and slurred. The rhythm resembles that seen in patients who are intoxicated by digitalis in whose electrocardiograms regular alternation in direction of the QRS complexes sometimes appears in attacks of tachycardia. The rate is 50-60. It is possible that auricular standstill is present.

Fig. 3 shows an almost complete attack of tachycardia, the tracing starting as soon after the onset as it was possible to start the electrocardiograph. During this attack the patient lapsed into unconsciousness as previously described. The first part of the record shows a regular diphasic oscillation of the string shadow at a rate of 230-250. There is a slow waxing and waning of the amplitude of the deflection. This phasic variation has been noted by Lewis[13] in experimental ventricular fibrillation. It is probably related to a change in electrical axis of the circulating wave in the ventricle as it alters its course. As the attack progressed the rate fell (in the second strip) to 210 and the complexes have more the form seen in paroxysmal ventricular tachycardia. The offset of the attack is abrupt after a recorded dura-

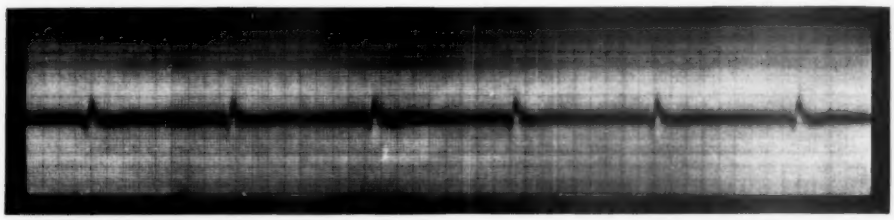

Fig. 5.—Record taken after patient had stopped breathing and was, to all appearances, dead. Rate 33 and regular. Probable auricular standstill.

tion of 32.8 seconds. A short period of gross arrhythmia follows, succeeded by a regular rhythm at a rate of 80.

A similar attack is shown in Fig. 4. The early part of this record shows a rate of 220, but this is reduced to 150 at the end of the paroxysm. Small waves present in the last strip suggest auricular activity, but many artefacts were caused by muscular movements of the patient.

Fig. 5 is an electrocardiogram taken after the patient had stopped breathing and was dead. It shows slow, regular, ventricular beats at a rate of 33 per minute. This cardiac action continued for several minutes after all other signs of life were absent.

DISCUSSION OF MECHANISM OF VENTRICULAR FIBRILLATION

The exact mechanisms acting in the human heart during ventricular fibrillation are as yet unknown. It seems clear, however, that the patient here reported was suffering from an abnormal rhythm best considered as fibrillation of the ventricles or perhaps more accurately as a preliminary rhythm to fibrillation, of the nature of ventricular

flutter. The predominating regularity of the oscillations at a rate not exceeding 250 is in favor of the latter diagnosis.

It is probable that the mechanism in ventricular fibrillation is similar to that known to occur in the auricles, and is produced by the development of a circus movement. The general character of the curves obtained is in favor of this hypothesis, and the forms of the different tracings recorded in the literature may represent stages analogous to those of fibrillation, flutter-fibrillation, and pure flutter of the auricles. The presence of highly specialized conducting tissues in the ventricles adds to the complexity of the circus movement when occurring in that chamber of the heart. An electrocardiogram published by Kerr and Bender[8] shows a very rapid and irregular oscillation of the string, at a rate of about 1000 per minute. This would more accurately correspond to what we call fibrillation in the auricles, in contrast to the slower and more regular rhythm recorded in our case.

QUINIDINE AND VENTRICULAR FIBRILLATION

Digitalis and quinidine have both been held responsible for ventricular fibrillation in man. Both drugs had been given in full doses to the patient we are reporting. In the case described by Kerr and Bender[8] attacks of syncope occurred in the course of quinidine therapy, and were shown by electrocardiograms to have been related to periods of rapid ventricular tachycardia, such as we are describing. An attack was initiated at one time in their case by the administration of 3.6 grams of quinidine sulphate in four days. In our patient 8.2 grams were given in four days.

The occurrence of unexplained death in the course of quinidine therapy has been the chief objection to its use. Because of this possibility this valuable drug has been discarded in many clinics. Attacks of syncope[8] have been noted in the course of quinidine therapy, and at least in two instances such syncope has proved to be associated with the onset of ventricular fibrillation. It has been shown[10] that the usual mechanism of quinidine death in cats is by respiratory paralysis. How often this mechanism has been responsible for death in man is unknown. More observations on the mode of death in higher mammals would throw light on this problem. As Garry[11] has shown, it is easier to produce ventricular fibrillation in the hearts of larger animals.

DE BOER'S THEORY OF QUINIDINE ACTION IN VENTRICULAR FIBRILLATION

The mode whereby fibrillation in the ventricles is produced is unknown. Lewis suggests that it may be the production of a circus movement through reëntrant ectopic beats. De Boer[12] has recently discussed the problem in an article entitled *Ventricular Fibrillation in Complete Heart-Block and the Action of Quinidine and Quinine Preparations in Heart-Block*. He emphasizes the fact that these preparations

alter the metabolic condition of the ventricular muscle so that variations in the refractory period occur irregularly in different parts of the heart, and permit of the development of a circulating wave from reëntrant ectopic beats. Moreover in auriculoventricular block the protecting influence of the His-Purkinje system is in abeyance. If intraventricular block is also present, the danger from quinidine in producing ectopic ventricular beats with circus movements is greatly increased.

De Boer appreciates what seems to us to be the important factor in the development of ventricular fibrillation, namely, the significance of the conducting system in preventing the development of circulating waves in ventricular muscle. His conclusions, however, are somewhat different from ours.

THEORETICAL FACTORS IN THE PRODUCTION OF VENTRICULAR FIBRILLATION

Let us first consider the physiological control normally operating to prevent an excitation, arising in the ventricular musculature, from going on to the production of circus movements in the ventricle. Extrasystoles are of common occurrence, but examples of reexcitation are infrequent.

Ventricular premature contractions are known to be followed by a compensatory pause which is due to a condition of refractoriness. This refractoriness is uniformly distributed over the entire musculature, and it is probable that such a generalized refractory state is responsible for the prevention of reexcitation and formation of circus movements. It is also probable that the uniform refractoriness of the ventricles as a whole is brought about by the elaborate conducting system in the ventricles: the bundle tissue, its branches, and the Purkinje fibers. An excitation that arises from a focus in muscle spreads in all directions and quickly reaches the endothelium and Purkinje fibers. Through these fibers it is quickly distributed to all parts of the ventricles. Conduction in ventricular muscle proceeds at a rate of about 450 mm. per second, whereas conduction in the Purkinje fibers varies from 2000 to 3000 mm. per second—from four to six times as rapidly. This permits an excitation spreading through the Purkinje fibers to intercept the excitation process spreading through muscle from the original focus, and in this way the entire muscle contracts almost simultaneously and is left in a generalized refractory state.

If it is allowed that the integrity of the bundle tissues and the Purkinje system normally prevents the formation of circus movement in the ventricles, then it would follow that depression, disease, or injury to these tissues would predispose or lead to fibrillation of the ventricles. This, we believe, is the chief factor. Both quinidine and digitalis are known to depress these tissues. However, in the cat quinidine usually kills by respiratory paralysis and digitalis by its

action on the ventricular muscle, before, according to the theory, the damage to the bundle tissue and Purkinje system, per se, is great enough to precipitate fibrillation.

Lewis[14] and his coworkers have studied the action of quinidine on the heart of the dog and demonstrated that quinidine greatly depresses the auriculoventricular node and bundle tissues of the dog's heart. A lengthening of the P-R intervals is regularly noted. A single dose of 0.1 gram given to dogs increased the QRS duration of the electrocardiogram by about 20 or 30 per cent. Repeated doses increased the time by 50 or 70 per cent. It is likely that quinidine in man has a similar depressing action on the bundle branch and Purkinje tissues.

In its action on the fibrillating auricles quinidine was found to (1) slow the rate of conduction, and (2) increase the refractory period. According to their experiments both actions were marked—an increase in the time of conduction and the lengthening of the refractory period amounting to about 100 per cent with large doses. The following factors will theoretically favor the continuation of circus movements in a muscle: (1) a long path or circuit, (2) a slow rate of conduction, (3) a short refractory period. In the fibrillating auricles the main path is usually confined to a ring about the great veins of the right auricle. In the ventricle, as far as is known, there is no one special circuit, and judging from the curves obtained, the circuit may be considerably longer than the path existing in auricular fibrillation. The rate of conduction in the ventricular muscle is approximately one-half the rate in the auricles (auricular rate 1000 mm. per second, ventricular rate 450 mm. per second). The longer circuit and the slower rate of conduction in the ventricular muscle favor circus movements by insuring a larger responsive gap. These conditions may be so favorable as to be but little influenced by quinidine. Further, the effects of its action on rate of conduction and the length of the refractory period tend to balance each other. This appears to explain why quinidine, a drug which abolishes fibrillation in the auricles, is unable to prevent the inception of fibrillation in the ventricles. On the contrary, by its depressing action on the bundle tissue and because of favorable conditions in the ventricles, fibrillation may be favored.

RELATION OF HEART-BLOCK TO VENTRICULAR FIBRILLATION

Five of 13 reported cases of ventricular fibrillation occurring in man were associated with complete heart-block as the underlying rhythm, either preceding or following the fibrillation. In the case reported here the rhythm, also, appeared to be governed from an infra-auricular center. All five cases with complete heart-block showed syncope or Adams-Stokes syndrome during the period of fibrillation. The question raised is how often is ventricular fibrillation the underlying mechanism in attacks of syncope known as Adams-Stokes syndrome. This

condition occurs in patients with disease of the bundle tissue and the usual supposition is complete ventricular standstill. As but few electrocardiographic studies have been made during such attacks, the frequency of ventricular fibrillation is unknown.

The poor prognosis in patients with disease of the bundle tissues suggests that coordinated ventricular action is dependent upon activity of the nodal centers situated in the bundle tissues. It would seem that with complete depression of these tissues ventricular action, save ventricular tachycardia or ventricular fibrillation, is impossible. This fact together with the noted association of heart-block and ventricular fibrillation is evidence in favor of the hypothesis presented above. From this theory it follows that a depressing drug acting on a bundle tissue already depressed by disease would find conditions favorable for the production of fibrillation. This seems to have been the situation in the case of Kerr and Bender and perhaps in the case we are reporting.

It is likely that depression of bundle tissues alone is the important precursor. The depression of the Purkinje system is of less importance for two reasons: (1) permanent ventricular rhythm governed by centers located below the bundles in Purkinje or muscle tissues is unknown, (2) depression sufficient to prevent simultaneous transmission from an active nodal center to all parts of the ventricle would have to be unusually extensive. The widespread Purkinje tissue is not as easily blocked as small centers confined to the bundle tissues.

THE MECHANISM OF CESSATION OF THE ATTACKS

The mechanism by which ventricular fibrillation is brought to a close remains to be discussed. We will recall that in our case the rhythm was governed from an infra-auricular center. An analysis of our tracings suggests that this center was not constant, but varied. It is apparent that the depression of the bundle tissues and Purkinje system that we hold responsible for the onset of fibrillation, recovered sufficiently to permit transmission. If this recovery took place in the presence of circus movements in the ventricular muscle, those circus movements would theoretically be brought to a close by the first excitation arising from the node and distributing through the Purkinje system to the musculature. This would destroy any responsive gap and result in a general state of refractoriness from which the ventricle would recover and permit the continuity of rhythmic control from the nodal center. As long as the nodal center and Purkinje fibers remained excitable, this rhythm would continue. With the reappearance of further depression, fibrillation might be precipitated again. The character of the tracings in the interfibrillation periods suggests incomplete recovery in the bundle-branch tissues.

De Boer believes that the intact conducting system prevents initiation of ventricular fibrillation in the normal heart by permitting the

diffusely distributed impulses of contraction to neutralize each other in all parts of the heart at one time. We would suggest that the development of a generalized refractory state of ventricular muscle following contraction brought about by a normal Purkinje and His system conduction is responsible for the prevention of reëntrant beats and circus movements. De Boer also believes that the cessation of an attack due to quinidine can be explained by a further action of the drug in so altering the refractory period that the circulating wave meets a wall of refractory muscle. A similar effect could occur with recovery and activity of the auriculoventricular node and conduction system. Impulses from node to Purkinje fibers would theoretically produce a totally refractory ventricular muscle, and thus end the circus movements. It is probable that quinidine has important actions on both ventricular muscle and conduction systems. It is our impression that influences on the latter are of major significance.

DIGITALIS AND VENTRICULAR FIBRILLATION

A corollary from this analysis would concern the part played by digitalis in the pathogenesis of ventricular fibrillation. It would appear likely that there is danger of precipitating such an abnormal rhythm by digitalis, in cases in which there is disease of the His bundle and its branches, by its depressing effect upon these tissues. Depression of the idioventricular center, especially if the branches of the bundle show evidence of lowered conductivity, would certainly favor such a rhythm. Moreover, this consideration would make it appear safer to omit digitalis during quinidine therapy, since the danger of inducing ventricular circus movements is minimized by the presence of an intact conducting system.

SUMMARY

1. A patient with rheumatic heart disease with syncopal attacks and death is reported with clinical, electrocardiographic and autopsy findings.

2. Electrocardiographic study showed the mechanism in the heart, during unconsciousness, to be a probable circus movement in the ventricles, of the nature of flutter or fibrillation, associated with auriculoventricular dissociation and auricular fibrillation or standstill.

3. The patient had received both digitalis and quinidine sulphate in moderately large doses. The possible influence of these drugs in initiating ventricular fibrillation by depression of the His-Purkinje system is discussed.

4. Patients with combined auriculoventricular and intraventricular block are particularly liable to ventricular circus rhythm if the conducting tissues are further depressed by digitalis or quinidine.

5. On theoretical grounds the use of quinidine to restore normal rhythm in auricular fibrillation would seem to be safer when it is not administered in combination with, or directly following digitalis. This conclusion is more definite when intraventricular block is present.

We wish to express our thanks to Dr. Ralph C. Larrabee for his permission to study and report this case.

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THE DEVELOPMENT OF THE ABNORMAL COMPLEXES OF THE ELECTROCARDIOGRAM IN CORONARY OCCLUSION*

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AT THE present time most clinicians believe that occlusion of a coronary artery is usually accompanied by a definite clinical syndrome. Herrick[1] in 1912 first accurately described in the American literature, the clinical signs and symptoms of this condition, which until that time had been confused with angina pectoris. The excellent papers of Longcope,[2] Wearn,[3] Hamman,[4] and many others in the last decade have led to a better definition of the signs and symptoms which follow sudden occlusion of a coronary artery with resulting infarction of cardiac muscle.

While contributions were being made to the recognition of the clinical syndrome accompanying this condition, investigators were studying, by means of electrocardiograms, deviations of the electrical currents which occur when cardiac muscle is injured by artificial means. Having this experimental basis, clinicians began to observe the changes in the electrocardiogram which take place when patients suffered from occlusion of a coronary artery.

In 1909 Eppinger and Rothberger[5] observed very unusual alterations in the electrocardiogram when an area of the left ventricular muscle of a dog was destroyed by the injection of silver nitrate into the cardiac wall. This change was characterized by marked alterations in the QRS complex, the R-T segment arising high on the descending limb of the R-wave. Gradual lowering of this segment followed until it became isoelectric. The final summit of the R-T segment was designated the T-wave by these authors.

Later, Samojloff[6] observed similar changes in the form of the electrocardiogram in experiments carried out on the hearts of frogs. When an area of muscle near the apex was traumatized, elevation of the R-T segment above the base line occurred. Such changes were of short duration, returning to normal on the death of the injured area of muscle.

In 1918, Smith[7] ligated branches of the coronary arteries of dogs; he observed similar rises in the R-T segment above the isoelectric level in a large percentage of his animals. He likewise designated the final summit of the R-T segment the T-wave and noted that in time it gradually approached the base line and finally became negative.

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In 1920, Smith[8] found that interruption of the blood supply to the apical region of the left ventricle gave the greatest exaggeration of this peculiar alteration of the electrocardiogram. He found also that ligation of the vessels supplying the right ventricle was not accompanied by these changes. Stewart[9] is of the opinion that at the present time a correlation cannot be demonstrated to exist between electrocardiographic signs and the specific coronary artery occluded. He arrived at this conclusion from a study of published records of patients dying of coronary occlusion in which the specific vessel involved was stated in the autopsy report together with the electrocardiographic changes which were observed. Otto,[10] however, has recently demonstrated that transient occlusion of a coronary vessel in dogs gives rather constant specific changes in the form of the electrocardiogram. It remains to be proved that such temporary occlusions have the same effect on the electrocardiogram as have the more permanent occlusions which occur in patients in the clinic.

Pardee[11] in 1920 obtained from a patient exhibiting the signs and symptoms which accompany occlusion of a coronary artery electrocardiograms which were somewhat similar to those which Eppinger and Rothberger[5] and Smith[7] had previously described. By inference Pardee concluded that the presence of distortion of the R-T segment was a sign of occlusion of a coronary artery. He further observed in this case that shortly after the alteration of the R-T segment the T-waves became inverted in all three leads. He also directed attention to the large amplitude and sharp spiking of the T-waves. Since the patient recovered and lived for two years, certainty of the pathological lesion which was present at the time of the attack is lacking.

In 1922 Kahn[12] intimated that increase in amplitude of the T-wave of the electrocardiogram, followed later by sharp inversion and gradual return to the isoelectric level, was a characteristic sign of coronary occlusion. His records also revealed the R-T segment in Lead I arising from the descending limb of the R-wave, slightly above the base line. At autopsy it was demonstrated that coronary thrombosis was the pathological lesion.

Wearn[3] in 1923 described certain alterations in the T-waves of the electrocardiograms derived from ten patients suffering from coronary occlusion. Because of the variety of changes which were observed he was of the opinion that no one form of the electrocardiogram was characteristic of this condition. The necropsy reports were combined in such a manner that individual pathological lesions could not be associated with corresponding change in the T-waves.

In 1923 Smith,[13] in reporting studies of eleven cases of coronary occlusion, included the report of a patient in whom the descending

branch of the left coronary artery had been ligated. The electrocardiogram obtained from this patient nineteen days after operation revealed negative T-waves in all three leads. They remained negative for a period of eight and one-half months; at the end of this time they were found to be positive in Leads I and II. Smith concluded from his observations on this series that decreased amplitude of the QRS complexes as well as changes in the T-waves were of diagnostic value.

Oppenheimer and Rothschild[14] in 1924, in a report of a series of cases of coronary occlusion that came to autopsy, placed emphasis on distortion of the R-T segment and the characteristic rise of this segment from isoelectric level. They noted that the distance between the R-T segment and the base line must be 0.1 millivolt to be of significance. They designated the second summit of the R-T segment the T-wave and observed that the T-wave became more separated from the R-wave by an upward convexity as the segment approached the isoelectric level. They called this convexity the "cove plane" T-wave. Pardee[15] in his series designated as "coronary T-waves" waves which were similar in form to those just described.

Willius and Barnes[16] in 1925 reported changes in the T-wave in eight cases of coronary occlusion. The most frequent change observed was negativity of the T-wave in Lead I; less frequently there was irregularity of this wave in one or both of the other two leads. Two patients in whom the electrocardiograms showed elevation of the R-T segments came to autopsy; occlusion of the coronary artery was the pathological lesion.

Recently, Parkinson and Bedford[17] published a series of twenty-eight cases in which they were of the opinion that the lesion was cardiac infarction following coronary occlusion. Six of the patients died; four of these came to autopsy; in these the clinical diagnosis was found to be correct. That is to say, cardiac infarction was the pathological lesion. As the most usual electrocardiographic phenomenon they observed deviation of the R-T and S-T segments of the ventricular complexes from the isoelectric line. The deviation usually measured 1.3 mm. but sometimes reached 6 mm. (10 mm. equal 1 millivolt). In the majority of their cases they found the R-T or the S-T deviation was best seen in Leads I and III. The deviations were always opposite in direction in these two leads. Elevation in Lead I was found to be as frequent in occurrence as depression.

In the experimental and clinical studies just reviewed, reference has been made to several authors who have designated as a T-wave the final summit of the R-T segment of their records. Parkinson and Bedford are of the opinion, however, that this portion of the R-T segment should not be so designated. They publish records in which definite T-waves appear before the R-T segment returns to the iso-

electric level. These T-waves are always opposite in direction to the initial deviation of the R-T segment.

Parkinson and Bedford from an analysis of the records of their own patients, as well as of those of others, express the opinion that the form which electrocardiograms assume following coronary occlusion falls into one of two main groups: in one group the T-wave is negative in Lead I and sharply positive in Lead III; in the other group the T-wave is positive in Lead I and negative in Lead III. They designate these groups the T 1 and T 3 types respectively.

There seems therefore to be evidence, experimental as well as clinical, that sudden closure of a branch of a coronary artery is usually accompanied by a change in the ventricular complex of the electrocardiogram. On searching the literature there is a surprising scarcity of complete series of electrocardiograms illustrating the types of changes that may occur in this condition and the transformation and development from day to day of various abnormal complexes that follow infarction of cardiac muscle.

It is our purpose to report the clinical course of a patient exhibiting the signs and symptoms of coronary occlusion, together with a series of electrocardiograms illustrating the progressive development of changes in the QRS and T-waves. These curves resemble closely the development of the T-wave schematically proposed by Parkinson and Bedford. We have failed to find in the literature a similar series of electrocardiograms which show the successive steps in the evolution of the abnormal waves which are said to be characteristic of this lesion.

CASE HISTORY

C. B., was a white man, single, 38 years old. He worked as a chauffeur. He was admitted to the hospital on Nov. 25, 1927, at 10 P.M., complaining of severe, stabbing precordial pain of two hours' duration. He was discharged from hospital on Jan. 13, 1928.

Present Illness.—The patient's illness began thirty-three hours before admission. While laying a carpet in his home he felt a sudden twinge of mild but sharp substernal pain. The pain did not radiate nor was it severe enough to cause him to stop work. It lasted about five minutes. Four hours later he experienced a similar attack while cranking an automobile. This attack was more severe than the first but was approximately of the same duration. He drove his car the remainder of the evening without difficulty. The next day he was free of symptoms. He was aware of nothing unusual except for slight loss of appetite. The following evening (two hours before admission to hospital) he was seized with very severe, stabbing substernal pain which did not radiate. He described it as "something squeezing his heart." He became dyspneic and went into a state of collapse. Pain persisted for one-half hour. He was given morphia 32 mg. in divided doses. Partial relief followed. Pain persisted while he was being moved to hospital; dyspnea likewise persisted but was not marked. He was nauseated.

Past History.—The patient had been well until the onset of the present illness. He did not recall being confined to bed before this. He had usually been active, but he had never worked at hard labor. He had experienced frequent mild attacks

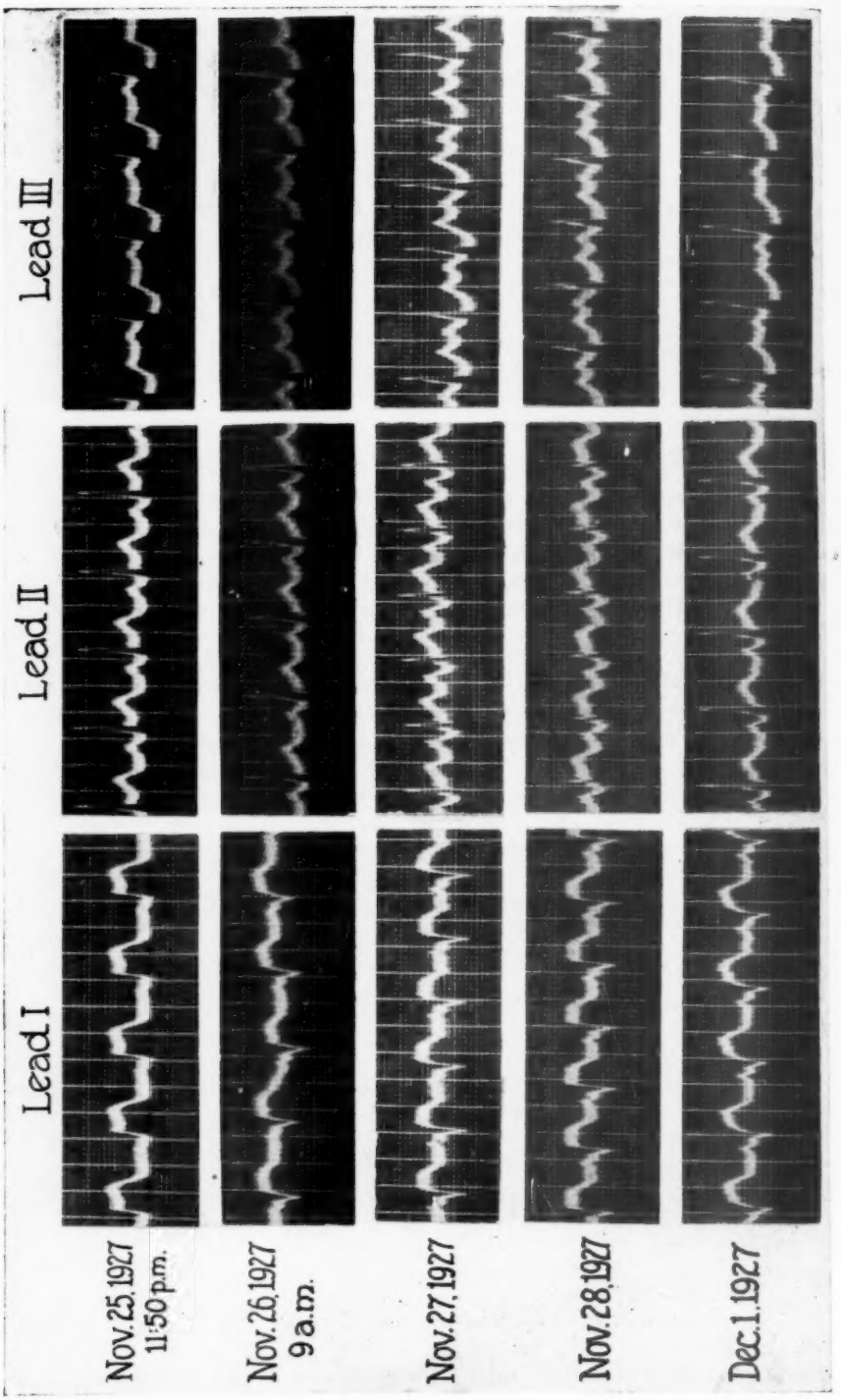
of headache for a number of years. He had been conscious of dyspnea on exertion during the past year. This symptom, however, had not interfered with his occupation. He had never experienced precordial pain nor palpitation. He had never been aware of the presence of edema. There was no history of gastro-intestinal disorders. The patient had gonorrhea at 22 years of age. There had been no recurrences. He had a chancre at 23 years of age, following which he was given several courses of salvarsan. No secondary symptoms of syphilis developed. Of two Wassermann tests made of the blood at the end of the antiluetic treatment, one had been negative and the other 4 plus. He used tobacco in moderation. He did not use alcohol.

Physical Examination.—The patient was an unusually large and well-developed white man. He appeared from ten to fifteen years older than his stated age. The skin was cold, moist and ashen gray. He was slightly dyspneic. The temperature was 100° F. (rectal), the pulse rate 90 per minute and the respirations 26 per minute. Eyes: There was slight bilateral arcus senilis. The pupils were equal and regular. They reacted promptly to light and in accommodation. The ears, nose and mouth appeared normal. There were no abnormal pulsations in the neck. The lungs were resonant throughout. There were a few fine moist râles at both lung bases posteriorly. Heart: There was no precordial thrill. The point of maximal impulse could neither be seen nor felt. The rhythm of the heart was regular; the rate was 90 per minute. The cardiac sounds were faint. There were no murmurs heard over the precordium. A friction rub was not present. The peripheral vessels were slightly thickened. The radial pulse was regular but weak. The systolic blood pressure measured 140 mm. of mercury, the diastolic 90 mm. The examination of the abdomen was negative. Extremities: There were no deformities. There was no edema of the feet. Glandular System: There was no generalized enlargement of the lymph nodes. Nervous System: The superficial and deep reflexes were present and normal.

Laboratory Examinations.—On admission to hospital, the urine showed a faint trace of albumin; the sediment was normal. The count of the white blood cells was 29,000, 92 per cent of which were polymorphonuclear in form and 8 per cent mononuclear. The count of the red blood cells was 4,800,000. The hemoglobin was 90 per cent (Dare). Fluoroscopic examination one hour after admission revealed that the lungs were clear and the hilus shadows were normal. The movements of the diaphragm were slightly limited on both sides. The heart did not appear enlarged. It occupied a transverse position. The aortic shadow was slightly widened. The Wassermann reaction of the blood at the end of the febrile period was negative.

Course in Hospital.—Immediately following fluoroscopic examination there was marked recurrence of pain. The radial pulse became weaker. The administration of morphia 16 mg. and nitroglycerine 0.64 mg. afforded considerable relief. The pain over the precordium continued throughout the night; it was, however, dull and less severe than during the evening. Pain continued for the next three days. The temperature ranged from 102° to 103° (rectal) during the first week, fell to 100° during the second, and then became normal. The pulse rate at first varied between 120 and 140 per minute and then fell to 100 per minute. The systolic blood pressure fell to 105 mm. and the diastolic to 80 mm., from having been at a systolic level of 140 mm. Certain changes occurred from day to day in the electrocardiograms (see description of electrocardiograms). The patient remained in bed for six weeks, began sitting up and walking during the seventh, and then went to the country for convalescence. He was free of symptoms on discharge from the hospital.

The patient returned to hospital twelve months later for examination. He had continued to work as a chauffeur. Dyspnea on exertion was still present; it


Lead I
Lead II
Lead III
Nov. 25, 1927 11:50 p.m.
Nov. 26, 1927 9 a.m.
Nov. 27, 1927
Nov. 28, 1927
Dec. 1, 1927

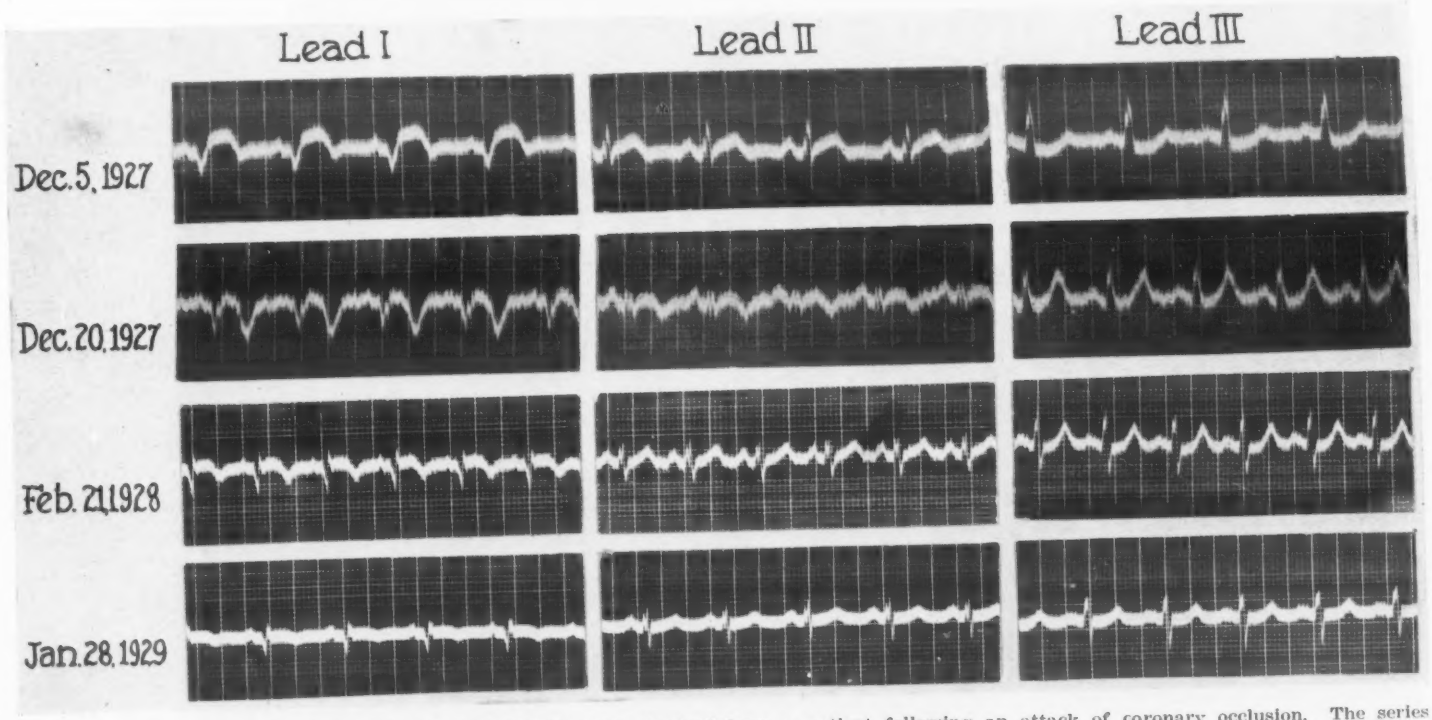


Fig. 1.—In this figure are reproduced electrocardiograms derived from a patient following an attack of coronary occlusion. The series illustrates the successive changes in the R-T and S-T segments and the evolution of the T-waves. For description see text. In these records the ordinates are 0.04 of a second apart; the abscissae 10^{-1} volts. The standardization in all records was such that 1 cm. equals 1 millivolt.

had not, however, increased in severity. He had experienced no cardiac pain. Examination of the heart was essentially the same as on discharge from the hospital except that over the pulmonic area there was distant slurring of the second sound extending into early diastole. The systolic blood pressure measured 122 mm. of mercury and the diastolic 78 mm.

The diagnosis* of this patient was.—Etiological: syphilis (?); anatomical: coronary occlusion; physiological: sinus rhythm.

Electrocardiograms.—The first electrocardiogram, taken four hours after the onset of the attack shows the R-T segment in Lead I originating directly from the peak of the R-wave (Fig. 1). There is a secondary rise in the segment which in records similar to this one has been designated a T-wave by some authors. Lead III in the same electrocardiogram shows a depression of the S-T segment and the beginning of the positive T-wave. Slight R-T elevation is seen in Lead II. Ten hours later (Nov. 26, 1927, 9 A.M.), the electrocardiogram is somewhat altered. In Lead I the R-T segment is of less amplitude; it is preceded by a well-defined Q-wave. There is no secondary rise which suggests a T-wave. Lead III shows an S-T depression with a well-defined positive T-wave. An S-wave is present in Lead II. There is little change in the electrocardiograms taken on Nov. 27, 28, and on Dec. 1. Ten days after the attack (Dec. 5, 1927) there is in Lead I a slight negativity at the end of the R-T segment, in that the R-T segment approaches the base line, crosses the isoelectric level for a short distance and gives an indentation below the line. This minute negative wave is the precursor of the negative T-wave. Lead III of this record shows slight notching of the QRS complex. The QRS interval, however, is only 0.06 of a second. On Dec. 20, twenty-five days after the first electrocardiogram, the T-wave in Lead I is sharply inverted and is preceded by the convex R-T interval. Oppenheimer and Rothschild[14] and Pardee[15] are of the opinion that this sign is characteristic of coronary occlusion. The only instance of T-wave negativity in Lead II is seen in this record.

The electrocardiogram, taken two months later (Feb. 21, 1928) reveals a negative T-wave of less voltage preceded by the "cove plane" in Lead I and a positive T-wave of less amplitude in Lead III. Notching of the R-wave is still present.

Fourteen months after the attack (Jan. 28, 1929) the electrocardiogram shows low voltage of all the complexes. The T-wave is slightly negative and traces of the former "cove plane" are still present. In Lead III there is notching of the R-wave and positive T-wave of low amplitude.

The P-R interval in all of the electrocardiograms of the series in 0.12 of a second in Lead I and 0.16 of a second in Leads II and III.

DISCUSSION

Clinical observers agree that pain, shock and dyspnea are the three characteristic symptoms of coronary occlusion. The pain is usually severe but varies in intensity with the size of the artery occluded. It is usually precordial in location, but it may radiate to the abdomen, in which case it may simulate an acute abdominal condition. It may be present for only a few hours or it may last for days. Shock is usually observed. Its severity varies with the size of the vessel which is occluded. Accompanying shock is an ashen gray appearance of the skin. A fall in blood pressure usually occurs a few hours after the onset; it may, however, occur earlier and remain low for several

*This diagnosis conforms to the nomenclature of cardiac diagnosis approved by the American Heart Association, AM HEART J. 2:202, 1926.

days. Dyspnea is usually present. It may be only transient and of slight intensity or may be so severe that the patient gasps for breath.

During the second twenty-four hours, fever and leucocytosis are always present. The fever varies from 100° to 102°, the count of the white blood cells from 12,000 to 20,000. Leucocytosis may persist from one to three weeks. Hamman[4] in reviewing the literature of the subject calls attention to other signs and symptoms which are present less constantly; to be mentioned are pericardial friction rub, suppression of urine, pulmonary edema, enlargement of the liver, albuminuria, and nervous symptoms.

The patient now being reported upon exhibited at the onset the cardinal symptoms of coronary occlusion, that is to say, pain, shock, and dyspnea. Shock, however, was not pronounced until twenty-four hours after admission. With persistence of pain, accompanied by a rise in temperature, leucocytosis and fall of blood pressure, the diagnosis of coronary occlusion appeared certain.

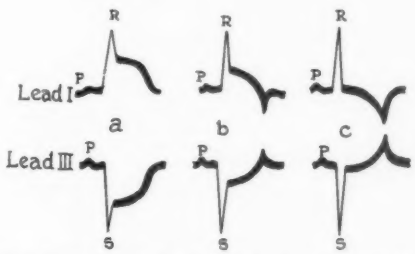


Fig. 2.—This figure is reproduced after Parkinson and Bedford. "Scheme illustrating the evolution of the plateau type of curve in Leads I and III. (*a*) Monophasic curve, reciprocal RS-T deviation in Leads I and III. (*b*) Intermediate phase, T-waves becoming evident. (*c*) Diphasic curve, T, of opposite sign in Leads I and III."

In the series of electrocardiograms of the patient taken on successive days can be traced the evolution of the plateau type of curve in Leads I and III such as was proposed by Parkinson and Bedford.[17] These authors devised a scheme which illustrates the successive stages. They were of the opinion that the ventricular complex is developed in three stages: the *monophasic* curve, the *intermediate* phase, and the *diphasic* curve (Fig. 2).*

The monophasic curve is seen in the electrocardiogram taken two hours after the occurrence of the coronary occlusion (Nov. 25, 1927). In Leads I and III there is reciprocal R-T and S-T deviation. The series falls therefore into the T-1 group. The first record indicates that the T-waves will eventually be negative in Lead I and positive in Lead III. The electrocardiograms taken on November 26, 27, and 28 further illustrate the monophasic stage, although a well defined Q-wave in Lead I and an upright T-wave in Lead III developed simultaneously ten hours after the first record. Three days later the R-T segment in

*We wish to thank Doctor Parkinson and Doctor Bedford for their kindness in giving us permission to reproduce this figure.

Lead I is convex; this is without doubt the precursor of the "cove plane" T-wave which is seen in the same lead in subsequent records.

The intermediate phase of the series is illustrated in the record taken on Dec. 5, 1927. The early negative T-wave is seen in Lead I as a negative depression of low amplitude after the R-T segment crosses the isoelectric level. The intermediate upright T-wave in Lead III developed before the corresponding wave in Lead I.

The diphasic curve illustrating the third stage in Parkinson and Bedford's scheme appeared in the electrocardiogram taken on Dec. 20, 1927. The sharply pointed negative T-waves of the "cove plane" type in Lead I and the similar but upright T-waves in Lead III are recognized as those often reported as being associated with coronary occlusion.

The changes which are seen to have occurred in the electrocardiogram three months after the occlusion (Feb. 21, 1928) are significant. If this record were examined alone, one would not suspect that marked alterations had occurred earlier in the R-, S-, and T-waves. That the curve is still of the diphasic type is of interest.

Fourteen months after the first record was taken (Jan. 28, 1929) all the complexes of the electrocardiogram are of low voltage. The only remnant which is left of the damage rendered by occlusion of a coronary artery is the slightly "cove plane" negative T-wave in Lead I.

Varying opinions have appeared in the literature as to the form which alterations of electrocardiograms of patients who have suffered from occlusion of a coronary artery assume. Wearn[3] expressed the view that there was no form typical of this condition. Another investigator[12] was of the opinion that most of the changes occurred in the T-waves. Abnormalities of the entire ventricular complex are, however, illustrated in the records of cases which have been reported.[11, 14, 15, 16, 17] Perhaps the confusion regarding the type of record associated with coronary occlusion is due in part to the varying lapses of time between the occurrence of the occlusion and the taking of the electrocardiogram. If this is correct, it is important that a larger number of complete series of electrocardiograms taken from patients who have suffered from occlusion of a coronary artery be published. It may be possible after a sufficiently large number of such series have been recorded to reconstruct the alterations in the electrocardiogram which have gone before and from a single record derive evidence that occlusion of a coronary artery had occurred at some earlier time.

SUMMARY

A report has been made of the case of a patient who exhibited the signs and symptoms which accompany occlusion of a coronary artery. Certain changes also occurred in the electrocardiograms. If these curves are arranged in serial fashion, the alterations which are ob-

served illustrate the evolution of the "coronary T-wave" in the manner that Parkinson and Bedford proposed in their scheme; that is to say, the monophasic, intermediate and diphasic stages which they described can be detected. No other series of records was discovered in the literature of this subject which illustrates these stages so exactly.

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THE OCCURRENCE OF THE CORONARY T-WAVE IN RHEUMATIC PERICARDITIS*

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SEVERAL observers have noticed that changes occur in the T-wave of patients who are suspected of having arteriosclerotic narrowing of the branches of the coronary system. One type of change has been observed immediately after thrombosis of a coronary branch and has been associated with cardiac infarction, while another type of change has been found to appear later after the infarction has had an opportunity to heal.[1] This latter T-wave abnormality has also been found in records of patients who have never had one of the severe attacks due to coronary thrombosis, but who have had the angina of effort which is associated with narrowed coronary branches.[2] This abnormality of the T-wave is seen in Fig. 1 and is characterized by a downwardly directed T-wave with the R-T or S-T interval showing an upward convexity, which lies either at the zero level of the record or above it. Changes in the T-wave or in the R-T or S-T interval have been reported by several observers as occurring in the course of acute rheumatic fever[3] and have been considered as evidence of myocardial damage caused by the rheumatic infection. In the course of study of a series of rheumatic patients in the wards of the city hospital, three patients have been observed whose electrocardiograms showed an abnormaliy of the T-wave which is practically identical with that described above as resulting from coronary narrowing, or following an infarction. These cases were all associated with a rheumatic pericarditis, and one of them came to autopsy.

CASE REPORTS

CASE 1.—A man, 48 years old, gave a somewhat doubtful history of rheumatism during his youth and had not had tonsillitis or sore throat to any extent. Before admission he had been ill in bed for one week, with what he called a cold. He was admitted complaining of marked shortness of breath with orthopnea and marked weakness. His temperature was 102° F., and his pulse was weak. His systolic blood pressure was 100 mm. and his diastolic 70 mm. The examination of the chest showed many rhonchi throughout. The heart sounds were distant and weak. There were no murmurs or pericardial friction rub. The liver was palpable four fingerbreadths below the costal margin. The Wassermann was negative. The x-ray examination showed considerable cardiac enlargement. The patient lived for three days, his temperature ranging from 100° to 103° F., and then he died.

The electrocardiogram taken the day before death is seen in Fig. 2. There is nothing noteworthy about the P-waves or the QRS group of this record except

*From the Medical Services and Cardiographic Department of the New York City Hospital.

the low voltage shown by the latter. The T-wave is turned downward in Lead I, and in the R-T interval there is seen an upward convexity which is much like that associated with localized coronary narrowing.

An autopsy was performed upon this patient, and the report from the pathological department by Doctor J. R. Lisa reads as follows: "The pericardium contains an excess of hemorrhagic fluid. The heart weighs 500 grams. The myocardiogram is hypertrophied and shows slight interstitial changes. The endocardium is smooth and shiny, and presents no abnormal features except for the valves. The mitral valve shows small, red, adherent vegetations about the size of a pinhead. The aortic valve is smooth and elastic and contains some sclerotic changes. The tricuspid valve is normal. The pulmonary valve is markedly sclerosed. The coronary vessels are patent and slightly thickened.

"*Microscopic:* The heart muscle of the left ventricle shows moderate hypertrophy. The mitral valve is thickened and fibrous. Beneath the epicardium is an

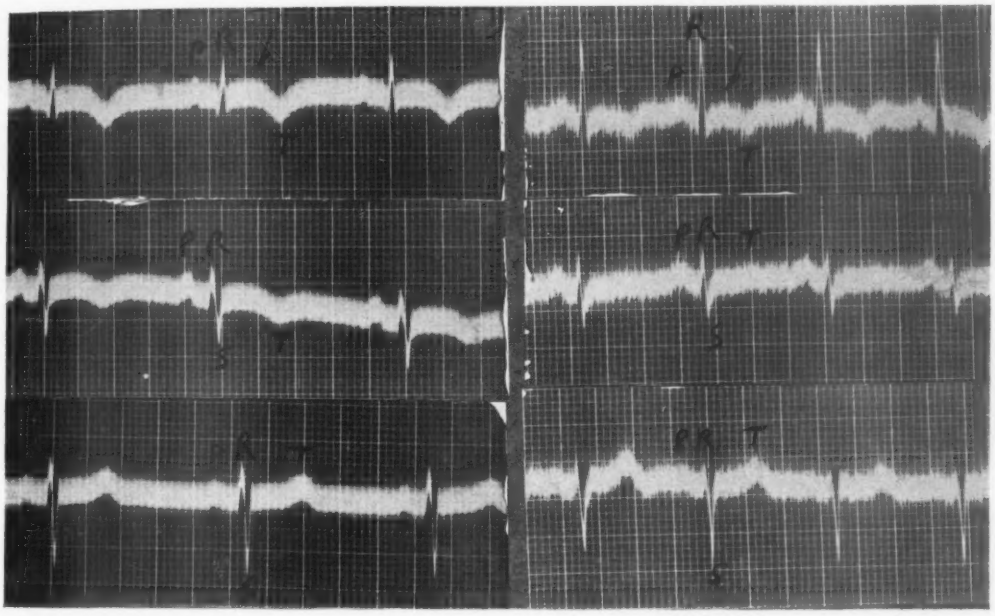

Fig. 1.—Records of two patients suffering from arteriosclerosis of the coronary arteries with the anginal syndrome appearing on effort. The upwardly convex portion of the R-T interval is indicated by the arrows.

early fibrous change with moderate cellular exudate. The left coronary artery is distinctly thickened and has an irregular subintimal proliferation. The fat around the coronary has a marked inflammatory reaction, especially beneath the epicardium. This reaction is focal, plasmocytic and lymphocytic in type. There are a few typical Aschoff bodies. The small blood vessels show moderate thickening, and there are occasional Aschoff bodies in their neighborhood. The wall of the left auricle is thickened, and there is subintimal proliferation with a mild inflammatory reaction in the outer portion of the left auricle. In the neighborhood of the pulmonary artery the pericardial reaction is very marked, becoming practically diffuse, and containing a great deal of hemorrhage. Small focal accumulations have lymphocytes, plasma cells and polynuclears interspersed by Aschoff cells. In addition there are Aschoff bodies. The muscle lying beneath this area shows several regions of inflammatory reaction and foci of early scar tissue formation."

CASE 2.—A man, 23 years old, gave a negative history for rheumatism in the past, and had had tonsillectomy two and a half years before because of frequent attacks of tonsillitis. He had been ill at home for a month, with sharp pains over the precordium, and weakness, but had not had to go to bed on this account. He was admitted on January 7, 1927, complaining of palpitation and weakness. On admission the temperature was 100° F., the pulse 82 and respirations 28. He was thin but did not appear particularly ill. His heart showed the cardiac dulness to extend 3 cm. to the left of the midclavicular line. The apex beat was not felt. The heart sounds were distant, and there were no murmurs heard. The systolic blood pressure was 100 mm. The Wassermann reaction was negative. The x-ray examination showed that the heart shadow was of triangular shape, suggesting pericardial effusion. An electrocardiogram taken on January 11 can be seen in Fig. 3. It shows the P-waves of low voltage. The auriculoventricular conduction time is normal, P-R measuring 0.18 second. The QRS group shows no special

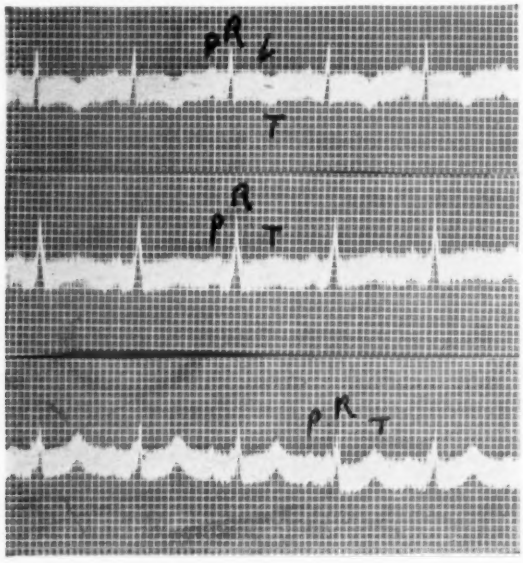

Fig. 2.—Record of Case 1.

abnormality. The T-wave is downward in Leads I and II, and in both leads there is an upward convexity of the R-T interval, like that seen in Figs. 1 and 2. A record taken on January 19 shows essentially the same characteristics as the earlier record. The upward convexity in Lead I is definite, and there is a slight degree of the same appearance in Lead II. During his stay in the hospital his afternoon temperature was frequently above 99° F., and occasionally above 100° F. He remained in the hospital thirteen days, and left against advice feeling well.

CASE 3.—A young man, 27 years old, was admitted on January 25, 1928. He had not been sick before this illness. Three weeks before he had felt weak and had had pain and swelling in the left knee, pain over the precordium and fever. On admission he appeared extremely sick, was short of breath and pale. His heart was enlarged to percussion, both to the right and left of the normal area. The rhythm was regular and the rate 94. The temperature was 103° F. There was a pericardial friction rub heard at the apex. The liver was felt 4 cm. below the costal margin. There was an acute polyarthritis involving several joints of the

extremities. The pericardial friction rub varied from time to time but disappeared completely after two weeks. He continued to have an up-and-down temperature. On February 28 he had a severe pain over the precordium, and at that time a systolic murmur was heard at the apex and a split second sound. At the aortic area a blowing diastolic murmur was heard. An electrocardiogram taken at this time is reproduced in Fig. 4. Frequent premature beats are seen, arising from the auriculoventricular node. The auricular waves (P) are normal. The auriculoventricular conduction time is normal; P-R measuring 0.18 second. The QRS group shows a slurring in Leads I and II, and a notching in Lead III. The T-wave is downward in Lead I and diphasic in Lead II, and in both of these leads there is an upward convexity of the R-T or S-T interval, which is similar to the appearance in Fig. 1.

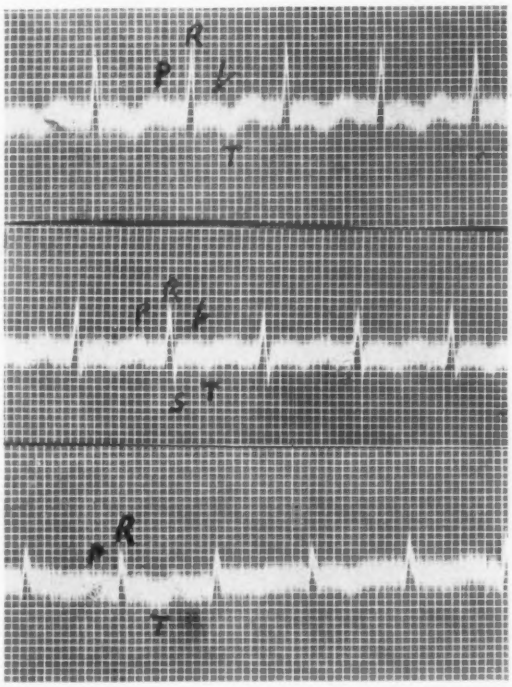

Fig. 3.—Record of Case 2.

Under antirheumatic treatment the fever gradually came down and the patient improved, until by March 21 he was free of symptoms. The electrocardiogram taken on March 26 is seen in Fig. 5. It will be noted that the QRS group is essentially the same, the nodal premature beats still are present, but that the T-wave is now upward in all three leads.

DISCUSSION

These three patients were all suffering from acute rheumatic pericarditis and myocarditis. In the first and third cases an endocarditis also was present, though in the first case it was not recognized during life. The abnormality of the T-wave, or rather of the R-T interval, observed in each of these cases is of special interest. The upward convexity of

this portion of the curve is very similar to that found in the records of certain patients who have had thrombosis of a coronary branch or who are suffering from marked coronary narrowing. Records showing this change in the T-wave, associated with coronary disease, have been reported by several investigators,[2] but in most of the reported records the voltage of the T-wave is greater than that shown in these three cases of rheumatic pericarditis. Occasionally, however, patients with coronary disease give records showing the upward convexity of the T-wave, and also a low voltage of the T-wave, so that from the electro-

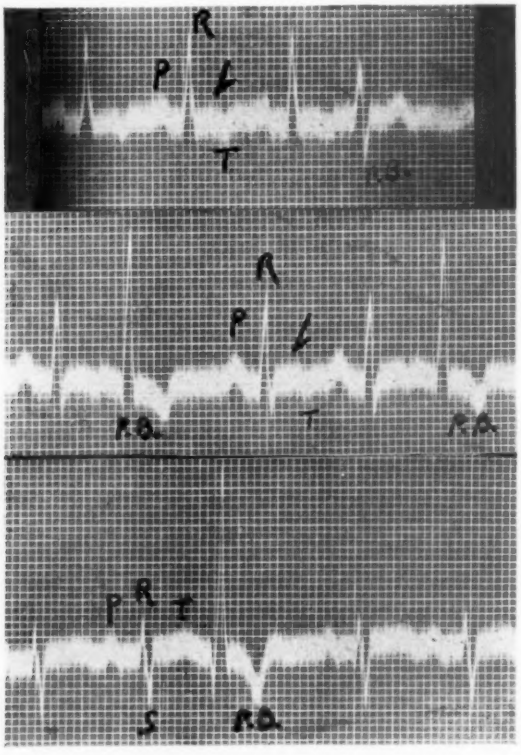

Fig. 4.—Record of Case 3 during the acute stage.

cardiogram alone it would be impossible to diagnose the condition from which the patient is suffering.

We believe that the T-wave abnormality observed in these three cases of pericarditis is due to a complicating myocardial inflammatory reaction. This indeed was found in the case which came to autopsy. We believe that this reaction gives rise to the change in the electrocardiogram, just as the myocardial degeneration, which results from coronary narrowing, produces a similar change in the records of patients with this condition.

It is to be noticed that in Case 3 the peculiarity of the T-wave had disappeared at the time of the second record, giving place to one which was almost if not quite normal. This return to a normal T-wave took place when the patient had clinically recovered from the rheumatic attack and probably indicates that the rheumatic process in the myocardium had subsided.

Changes in the T-wave and in the R-T interval have been reported as occurring in the course of acute rheumatic fever by Cohn and Swift;[3] by Rothchild, Sacks and Libman,[3] and by others. It has not, however, been noted that an upward convexity of the R-T interval like that found after coronary narrowing or occlusion may also occur as a result of rheumatic, myocardial affection. In Fig. 8 *a*, of the article

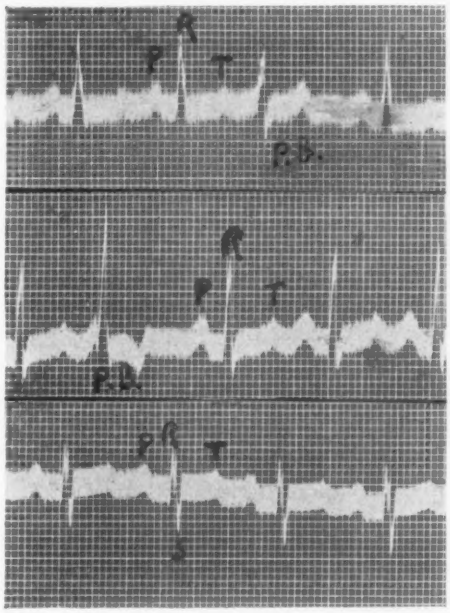

Fig. 5.—Record of Case 3 after recovery.

by Cohn and Swift (patients with rate 102 and 107 respectively), there are two tracings which show this feature; and one of them (rate 107) shows in addition a considerable voltage of the T-wave. It does not appear in this article, however, to which cases these tracings belong, so that we cannot say whether or not these patients had pericarditis.

The similarity of the T-wave in these two conditions, whose pathology is so dissimilar, throws an interesting light on the mechanism of alterations in the form of the T-wave. The fact that quite dissimilar pathological changes may affect the T-wave similarly is not at all discordant with our present understanding of this wave, for it is likely that the location of the damage is of more importance than the damag-

ing agent. It would be interesting if pathological studies should show that a certain location of the disease will cause these changes in Lead I, and that a different location will affect Lead II. So far we have been unable to substantiate this, because of inability to make a sufficiently detailed study of the heart to demonstrate in what areas of the ventricular musculature the disease is most intense. It does not seem unlikely that similar T-wave changes may occur as a result of acute rheumatic myocarditis without the complication of pericarditis, and studies are in progress to elucidate this fact.

We wish to express our thanks to Dr. Orrin S. Wightman and to Dr. Peter Irving for the privilege of reporting these cases which occurred on their services at the city hospital.

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THE AURICULAR BLOOD SUPPLY IN THE DOG

I. General Auricular Supply With Special Reference to the Sino-Auricular Node*

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ALTHOUGH much experimental work has now been done on the specialized tissues of the dog's heart, the blood supply to these structures has never been very carefully investigated. Information of this kind became necessary to us in the pursuance of a physiological problem involving a reduction in the blood supply to the sino-auricular node. The present observations were made in this connection.

The coronary supply to the ventricular portions of the heart has long been a subject of detailed study. The auricular portions have, however, been generally neglected. The full significanec of the vascular distribution to the auricles was realized with the discovery of the sino-auricular and atrioventricular nodes. Of all those who have worked on the coronary circulation since that time the most outstanding and the only ones to whom we need specifically refer are Keith and Flack,[2] Koch,[3, 4] Gross,[1] and Spalteholz.[5] In the monograph of Spalteholz a complete bibliography may be found.

As far as the sino-auricular node is concerned these workers completely agree on only one point, namely, that the node has its own special nutrient artery. As to the branches of the coronary which supply this sino-auricular artery, there is much divergence of opinion. In this discussion the terminology of Spalteholz will be used since it is comprehensive enough to include all the arteries described by the other workers. Spalteholz recognizes three main branches to each auricle which arise from the respective coronaries. Each of these branches is termed ramus atrialis, dexter or sinister, and specifically anterior, intermedius or posterior according to its proximity to the origin of the coronary itself.

Keith and Flack, who first described the sino-auricular node, note in man a sino-auricular arterial circle surrounding the superior caval funnel. The portion of this lying in the sulcus terminalis supplies the sino-auricular node. This circle is developed from the ramus atrialis dexter anterior and the ramus atrialis dexter intermedius. There is also an anterior anastomosis with a branch of the left coronary, very evidently the ramus atrialis sinister anterior.

According to Koch also there is an arterial circle around the superior caval funnel which is developed from two branches of the right coro-

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nary. An ascending branch mesial to the right auricular appendage sends a small twig to the appendage caval angle, while the main branch passes around the superior vena cava reappearing on the dorsal surface of the right auricle and entering the sulcus about where the stem of the sinus node ceases. Here it joins a branch of the right coronary which has come up the dorsal wall of the right auricle. The united branches penetrate the sinus node as the sinus node artery. It is evident that Koch is describing the course of the ramus atrialis dexter anterior and the ramus atrialis dexter intermedius. Whether or not the ring is entirely closed by an anastomosis between the sinus node artery and the small twig which passed through the appendage caval angle is not clear. In his later description Koch notes that the mesial branch usually makes anastomoses with branches from the left coronary.

Gross finds with great constancy an arterial ring around the superior caval funnel, and the vessel from which it arises he terms the ramus ostii cavae superioris. This vessel may arise in 60 per cent of the cases as a stout branch of the right coronary soon after its origin, in which case we recognize it as the ramus atrialis dexter anterior. In 40 per cent of the cases Gross finds it originating from the left coronary, very evidently as the ramus atrialis sinister anterior. Although Gross mentions that his ramus ostii cavae superioris when arising from the left coronary may anastomose after reaching the external surface of the right auricle with other auricular branches, he states that there are never two rami ostii cavae superiores, which seems to indicate that he does not believe the sino-auricular node itself is ever directly supplied by anastomoses from both coronaries.

In a series of twenty human hearts figured in his monograph Spalteholz finds a sino-arterial ring in only six cases. In only one of these does the ring receive a branch from the other coronary, such as described by Keith and Flack. In four cases the ring is formed by branches of the left coronary and in two cases by branches of the right. Five times the sino-auricular node is supplied by the ramus atrialis sinister anterior, three times by the ramus atrialis sinister intermedius, nine times by the ramus atrialis dexter anterior and twice by the ramus atrialis dexter intermedius.

METHODS

Although the course of arteries in a limited region may be best studied by serial sections, these are not suitable for following the origin and distribution of entire coronary branches. For this purpose there is apparently no substitute for some kind of an injection method. We have followed the technic of Gross rather closely, using the barium sulphate injection mass. After rigor had passed off, the hearts were thoroughly washed through the coronaries with normal saline. Both washing and injection were done under 150 mm. to 160 mm. Hg. pres-

sure and in a chamber kept at approximately 37° C. Keeping the heart warm during the period of injection was a matter of greatest importance. After the injection was complete, the heart was chilled in cold water and then placed in formalin. Dehydration was brought about by alcohols of increasing strength, the specimens being left in absolute alcohol for several days. Clearing took place in synthetic oil of wintergreen. In the dog the left coronary divides into its two main branches so soon after leaving the aorta that often a cannula was inserted into each branch. By means of Y-tubes all three injection cannulas were then connected to the single pressure bottle.

Our first intention was to study the specimens by means of x-ray pictures. It was soon evident that this was a difficult procedure in the thin walled auricles. From the x-ray pictures it was impossible to tell whether two vessels branched or merely crossed each other. The injected vessels stood out with such contrast to the eye that we finally distended the auricles with strips of dark colored cloth, inserted through the vena cava and tips of the appendages, and made our observations with the binocular microscope. A magnification of from 10 to 20 times brought into view all vessels with their branches and anastomoses down to the smaller arterioles. After becoming familiar with the technic of injection our preservations were uniformly clear and beautiful.

Whitten[6] has recently critically reviewed the injection methods for study of the coronaries. Whatever objections there may be to these methods as applied to the heavy walled ventricles they are eminently satisfactory for the thinner auricles.

THE AURICULAR BLOOD SUPPLY

The distribution of the coronary branches to the auricles may be seen in Figs. 1 and 2. These figures somewhat diagrammatically represent the auricular blood supply as found in 39, or 73 per cent, of 53 dog hearts. The terminology and scheme of numbering used by Spalteholz has been retained but extended where necessary. A brief description of the main branches of each coronary follows.

Ramus atrialis dexter anterior.—This branch (3 in Fig. 1) arises from the right coronary soon after the latter's origin from the aorta. In 49 of our 53 cases it has what Spalteholz terms a weak development; that is, it passes upward over the aortic surface of the right auricle and then distributes itself principally to this region and to the aortic surface of the right appendage. It never anastomoses with any of the other branches which adjoin and somewhat penetrate its territories. This ramus often passes over the margin of the appendage and supplies some of its dorsal and lateral surfaces.

In almost all our specimens another strong branch arises either close to the aorta (3a in Fig. 1) or directly from the right anterior as indi-

cated by the dotted lines in Fig. 1. We have called it the right anterior accessory. It curves around the aorta, supplying the immediately adjacent areas, and then passes transversely across the anterior surface of the right auricle. Some of its branches seem to enter deeply into the interauricular muscular band and so pass on into the septum, although this has not yet been carefully worked out.

In four of the hearts this ramus atrialis dexter anterior accessorius has been very strongly developed. This development is always associated with a very small ramus atrialis sinister anterior. The result is that the accessory branch supplies the entire field ordinarily taken care of by the left anterior. It anastomoses with the right intermedius on both sides of the superior vena cava, sends branches to the areas surrounding the pulmonary veins where it joins branches from the ramus atrialis sinister posterior, and finally it anastomoses with

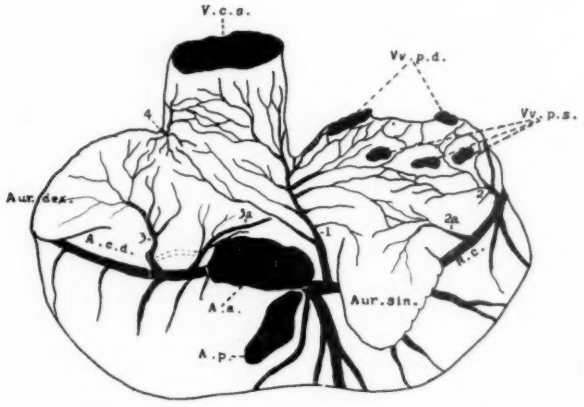

Fig. 1.—Anteroventral view of the auricular regions. The following abbreviations and numbers apply to all figures. V.c.s., superior vena cava; V.c.i., inferior vena cava; Aur. sin., left auricular appendage; Aur. dex., right auricular appendage; A.c.d., right coronary; R.C., ramus circumflex of the left coronary; Vv.p.s., left pulmonary veins; Vv.p.d., right pulmonary veins; A.a. aorta; A.p., pulmonary artery; 1. Ramus atrialis sinister anterior; 2. ramus atrialis sinister intermedius; 2a. ramus atrialis sinister intermedius accessorius; 3. ramus atrialis dexter anterior; 3a. ramus atrialis dexter anterior accessorius; 4. ramus atrialis dexter intermedius; 5. ramus atrialis dexter posterior; 6. ramus cristae terminalis; 7. ramus atrialis sinister posterior; 8. rami pulmonales sinistri anterioris.

branches from the ramus atrialis sinister intermedius on the anterior aspect of the left auricle. This distribution is so uncommon that it may be termed an anomaly. It is illustrated in Fig. 3.

Ramus atrialis dexter intermedius.—From the right coronary at about the middle of the right auriculoventricular boundary there arises a branch, usually stout, the ramus atrialis dexter intermedius. In 81 per cent of our cases its course is as follows: it first passes transversely across the body of the right auricle then bends sharply forward and finally runs fairly directly to the angle between the superior vena cava and the right appendage. On its way it sends off branches which anastomose with left coronary branches around the right pulmonary

veins. Occasionally its branches extend beneath the inferior vena cava and join arteries from the left coronary in this region. It also sends branches to the left around the superior vena cava which join branches of the left anterior. The main stem transverses the sulcus terminalis and reaches the ventral surface of the auricle by way of the notch between the vena cava and appendage. It does not extend far on the ventral surface but interdigitates with branches of the right and left anterior. In addition it always anastomoses with the left anterior. Sometimes this occurs so directly that it is impossible to say which artery passes from one side to the other. Usually the anastomoses occurs above the sulcus terminalis on the right side of the superior vena cava. Since branches of the right intermediate anastomose with the left anterior on both sides of the vena cava it is

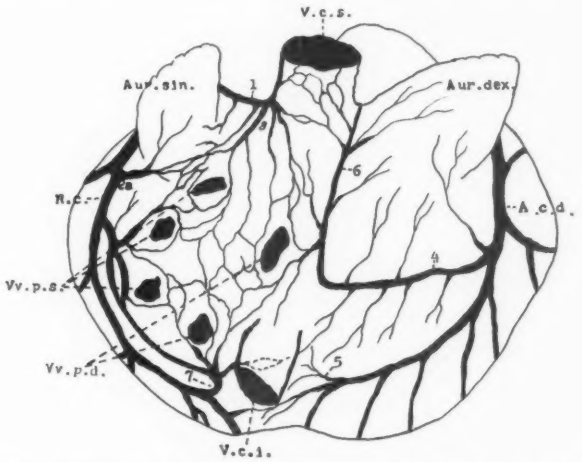

Fig. 2.—Dorsal view of the auricular portions of the heart. The drawing is partially diagrammatic in that the right and left sides have been brought into the same view, somewhat in the manner of a Mercator projection.

obvious that an arterial ring is thus formed around the superior caval funnel.

In forty-three of our fifty-three cases the right intermediate has the above distribution. In all of these it may be said to supply the sinus node since it transverses the sulcus terminalis. Figs. 1 and 2 illustrate the above description.

In eight specimens we have found the right intermediate weakly developed, its place being taken by the left anterior. This condition will be described under that heading.

An unusual development of the right intermediate was found in two hearts. Not far from its origin the artery divided into two large branches, one passing along the sulcus terminalis and through the angle between the superior vena cava and appendage, the other passing between the vena cava and the right pulmonary veins. Both branches thus reached the anteroventral surface where they anastomosed with each other and supplied part of the region usually taken

care of by the left anterior. Anastomoses with the left anterior were also present.

Ramus atrialis dexter posterior.—In the dog this artery is poorly developed and distinguished with difficulty. It reaches the areas on the right side of the inferior vena cava, and under this vein it sometimes anastomoses with branches from the left coronary.

Ramus atrialis sinister anterior.—This branch arises from the ramus circumflexus soon after its origin from the left coronary. It has had a strong development in all except four of our hearts where as already related it was largely replaced by the accessory branch of the right anterior. After its origin the left anterior passes to the left and forward sending large branches to each side of the superior vena cava. It anastomoses freely with the right intermediate usually on the right side just above the vena cava appendage angle and on the left side in

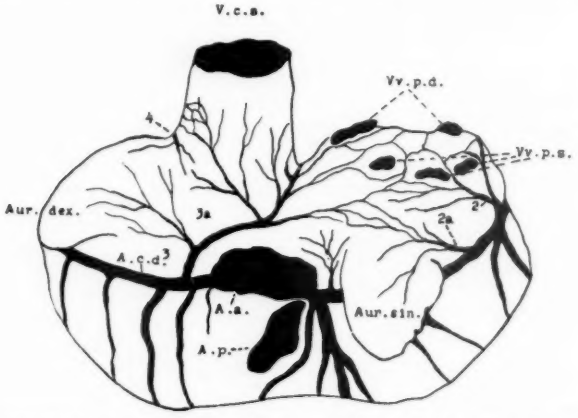

Fig. 3.—Anteroventral view of the auricular regions showing the strong development of the accessory branch of the right atrialis dexter anterior.

the notch between the vena cava and the right pulmonaries. Three or four branches to the left join the plexuses around the pulmonary veins which are made up of branches from the left intermediate and left posterior. There is never any anastomosis with the ramus atrialis dexter anterior. The usual distribution of this artery may be seen in Fig. 1.

In eight of our specimens the left anterior has been unusually strongly developed. The branches that passed to the sides of the superior vena cava extended through to the dorsal surface and supplied the field ordinarily taken care of by the right intermediate including the sinus node itself. There were no anastomoses with the right intermediate on the body of the right auricle, but union did occur in the region of the pulmonary veins. Fig. 4 illustrates the dorsal view of one of these cases.

Ramus atrialis sinister intermedius.—From the lower edge of the left auricle just beyond the appendage two branches arise from the

ramus circumflex of the left coronary, which supply the left appendage and those areas of the left auricle adjacent to the left pulmonary veins. The second of these arteries is usually the larger, and it may be properly called the left intermediate, the first one being conveniently termed the accessory. These arteries may be noted as 2a and 2b on any of the figures. Both the accessory and the intermediate itself anastomose with branches of the left anterior at the base of the left appendage. In the four cases already described in which the left anterior was replaced by the accessory branch of the right anterior there was an anastomosis between this artery and the left intermediates.

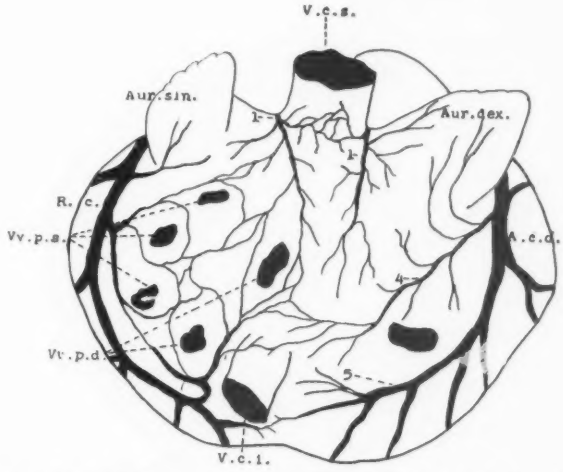

Fig. 4.—Dorsal view of the auricular portions of the heart showing the marked development of the ramus atrialis sinister anterior which has sent two large branches over on the dorsal surfaces. The right intermediate is only moderately developed supplying only part of the right appendage and the lower part of the right auricle.

The left intermediate contributes numerous branches to the plexus of arteries which surround the pulmonary veins. One large branch regularly swings to the right around the base of the left auricle and joins the left posterior. The left intermediate is very regular in its distribution, no variations worth recording being noted in any of our specimens.

Ramus atrialis sinister posterior.—In the angle between the left auricle and the inferior vena cava is regularly found a branch of the left coronary which joins the plexus around the pulmonary veins. It also anastomoses with the right intermediate both on the posterior surface where the two auricles meet and underneath the inferior vena cava. The course of this artery may be seen in Fig. 2.

Ramus cristae terminalis.—This name Spalteholz gives to the artery which penetrates the crista terminalis of the right auricle. In the human heart according to Spalteholz's drawings it was formed nine times from the right anterior, five times from the left anterior, three times from the left intermediate and only twice from the right inter-

mediate. In the dog's heart we have found this artery arising forty-five times from the right intermediate and eight times from the left anterior. Not once has the right anterior passed through the caval appendage angle, as in the human heart, to form this ramus. This artery is numbered 6 in our drawings. The importance of this artery is due to the fact that it lies in the boundary between the sinus and atrium. This region has great physiological significance, for its upper end contains the sinus node. The artery that forms the ramus cristae terminalis, therefore, also supplies the sinus node.

Arterial ring around the superior vena caval funnel.—Keith and Flack emphasized the presence of an arterial ring around the opening of the superior vena cava into the right auricle. According to their drawings this ring was formed by the right anterior and the right intermediate. Spalteholz found such an arterial circle in only about one-third of his specimens. Three times the ring was formed by the right atrialis sinister anterior, once by the right atrialis sinister intermedius, once by the right atrialis dexter anterior and once by the right atrialis dexter anterior in anastomosis with the right atrialis sinister anterior. We have not found a ring as well marked as indicated in Keith and Flack's drawings, but in all our specimens there is a series of anastomoses around the caval funnel. In thirty-nine cases the ring is formed by anastomoses between the right intermediate and the left anterior as may be seen in Figs. 1 and 2. In eight cases the ring is formed by the left anterior alone as illustrated for the dorsal side in Fig. 4. In four cases the ring is formed by the right anterior accessory and the right intermediate. In two cases the ring is formed by the right intermediate alone. In the dog, therefore, an arterial ring around the caval funnel is constant, and in the majority of cases it is formed by branches from the two coronaries. Even when formed by one artery, somewhere beyond the ring there are invariably anastomoses with other arteries. In Fig. 4 the left branch of the left anterior finally joins the plexus around the pulmonary veins as well as the right intermediate near the inferior vena cava.

Blood supply to the sinus node.—The sinus node is supplied by the right side of the above described arterial ring. The large artery forming this portion of the ring continues as the ramus cristae terminalis. Since the arterial ring is formed either by two separate arteries, or by one artery which later anastomoses with its neighbors, the sinus node is furnished with an abundant and sure blood supply. Preliminary experiments made before the blood supply to the node was known in detail showed that it was extremely difficult to reduce its circulation sufficiently to cause injury. Likewise auricular thrombi are seldom if ever found in the region of the sulcus terminalis. The explanation for both facts is readily found in the anastomosing blood supply.

SUMMARY AND DISCUSSION

By means of barium sulphate gelatin injections the auricular blood supply has been studied in fifty-three dogs' hearts. In forty-five of these the sinus node was supplied by the ramus atrialis dexter intermedius, the second auricular branch of the right coronary. In eight hearts it was supplied by the ramus atrialis sinister anterior, the first branch of the ramus circumflexus of the left coronary.

Although the sinus node artery came directly from the branch just named, there was in all cases studied an arterial ring formed around the superior caval funnel. In thirty-nine cases this ring was formed by anastomoses between the right intermediate and the left anterior, in four cases by anastomoses between the right intermediate and the right anterior, in two cases by the right intermediate alone, and in eight cases by the right anterior alone. In the ten hearts in which a single artery formed the arterial ring there were anastomoses beyond the ring with branches from the opposite coronary. The sino-auricular node could thus always be supplied either directly or indirectly from both coronaries.

The dog's heart has certain regions in which anastomoses do not seem to occur but others in which they are particularly abundant. Of the latter, the superior vena caval funnel has been sufficiently discussed. Fig. 2 shows the rich connections between all the coronary branches that supply the body of the left auricle. The inferior vena caval funnel is very poorly supplied as compared to the superior. There is, however, often an arterial ring made by branches from the left posterior and the right intermediate. The area just ventral to the inferior vena cava in the neighborhood of the coronary sinus is rather well supplied. Anastomoses here occur between the left posterior and right intermediate as well as direct connections between the ramus circumflex and right coronary. Most of these regions have special phylogenetic significance. They are in part boundaries between parts of the heart which have different origins, and in nearly all of them specialized automatic and conductive tissue has been found, either in small scattered masses or in large concentrated nodes.

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THE BUFFER FUNCTION OF THE DIAPHRAGM AND THE CARDIO-ABDOMINO-DIAPHRAGMATIC SYNDROME*

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INTRODUCTION

IN ADDITION to its respiratory function the diaphragm serves as a buffer between the thoracic and abdominal cavities where the pressure is subject to considerable physiological variations. According to A. Bernou,[1] the intra-abdominal pressure varies, not only with the respiratory movements but also with changes in the position of the body. Thus it may vary between 10 and 35 cm. of water during expiration and from 15 to 45 cm. during inspiration, or from 10 to 2 cm. with relaxation of the abdomen.

We shall not consider the extreme variations in intra-abdominal pressure caused by such conditions as pregnancy, tumors, ascites, tympanites, etc., because in such cases the protective function of the diaphragm is of secondary importance. In the ordinary physiological variations in intra-abdominal pressure (variations caused by changes in position, filling the stomach, emptying the intestine, etc.) the diaphragm adequately serves its function of protecting the thoracic organs, especially the organs of the circulatory system, against the harmful effects of variations in intra-abdominal pressure. While the intrathoracic pressure is subject to even more marked physiological variations, caused by respiration and to a lesser extent by the action of the heart, the rôle of the diaphragm in respiration is direct and active. The influence of the respiratory movements of the diaphragm on the abdominal cavity is modified by the combined diaphragmatico-abdominal reflex of Sherrington, that is, by the antagonistic action of the diaphragm and the muscles of the abdominal wall. It is perhaps more accurate to speak, not only of the moderating influence of the diaphragm on the physiological variations of pressure in the abdominal and thoracic cavities, but of a system in which the reciprocal action of the diaphragm and the abdominal muscles is of primary importance. We shall not discuss the question of the part played by the muscles of the thoracic cage, for that is outside the plan of the present study.

The protective action of the diaphragm is the result of variations in the tone of the muscle, and according to Kure, Hiamatsu and Naïto,[2] this tone depends on the sympathetic nervous system, impulses being carried by the splanchnic nerve. That is in accord with the teachings of the school of Prof. L. A. Orbeli[3] that the tone of striated muscles

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depends on the sympathetic system. (See the reports presented at the Congress of Physiologists at Leningrad in 1926.) Similar views are expressed by Backe,[4] de Boer[5] and others.[7] Felix,[6] after extirpation of the sympathetic ganglia related to the diaphragm, observed changes in the latter similar to those met in progressive muscular dystrophy; in the case of complete separation of the diaphragm from the sympathetic system he even observed complete degeneration of the muscle fibers. These findings are in perfect accord with the teachings of Prof. J. P. Pavlov[7] on the trophic function of the sympathetic nervous system. But after all it is hard to believe that the tone of the diaphragm, which functions rhythmically, should depend only on the sympathetic nervous system. According to Frank[10] the parasympathetic system, represented by fibers corresponding to the phrenic nerve, is concerned with relaxation of the diaphragm.

In many ways the function of the striated muscle of the diaphragm seems distinct from that of other striated muscles and in some respects resembles the heart muscle. According to Starling[8] the contraction of the diaphragm lasts from four to eight times longer than does that of any other striated muscle. It seems that this muscle periodically goes into a state of tetany for a short time. If we recall that with respiration the diaphragm maintains a more or less pronounced rhythmic action which continues uninterruptedly throughout life, varying only in degree, we have reason for separating the muscle of the diaphragm, as well as that of the heart, from other striated muscles. We may assume that the tone of this muscle is the result of interplay of the sympathetic and parasympathetic systems. In this connection experiments made by W. M. Bayliss[9] on the effect of cutting the vagus on the tone of the diaphragm are of great interest. It is important to realize, however, that the question of the nervous regulation of the tone of the diaphragm is not finally settled (Kahn[12]).

Frohlich and Meyer[11] speak of a particular tonus system which maintains the tone of the diaphragm directly without being interrupted by ganglia. However that may be, there are reasons for believing that the tone of the diaphragmatic muscle is maintained by the autonomic nervous system and that it must be affected by reflexes from different organs, as the effector link in a whole series of reflex arcs where various organs may serve as receptors. In our observations on the tonotropic reflexes of the heart we have encountered reflexes similar to those of the diaphragm. We have been able to study the following reflexes of the diaphragm:

1. The reflex of filling the stomach (reflex of intragastric pressure).
2. The reflex of pressure on the eyeballs (oculocardiac reflex).
3. The reflex of change from orthostatic to clinostatic position (clinostatic reflex).
4. The x-ray reflex.

METHOD OF STUDY

We did not introduce the roentgenoscopic method in the routine of studying the reflexes, nor did we admit it in our study of the tonotropic cardiac reflexes. The reasons for not using this method are illustrated by Fig. 3 which represents the outlines of the heart and the cardiophrenic angles as determined by percussion, with the patient in the orthostatic position; (1) control, (2) after pressure on the eyeballs and (3) under the influence of the x-rays. From this we see that the effect of the x-ray is similar to that of pressure on the eyeballs, and that the shadow on the screen corresponds with the contour as determined by percussion. The reflex change is seen as a lowering of the diaphragm (determined by the cardiophrenic angles); that is, with these two reflexes there is an increase in the tone of the diaphragm. As the use of the fluoroscope always has this reflex effect on

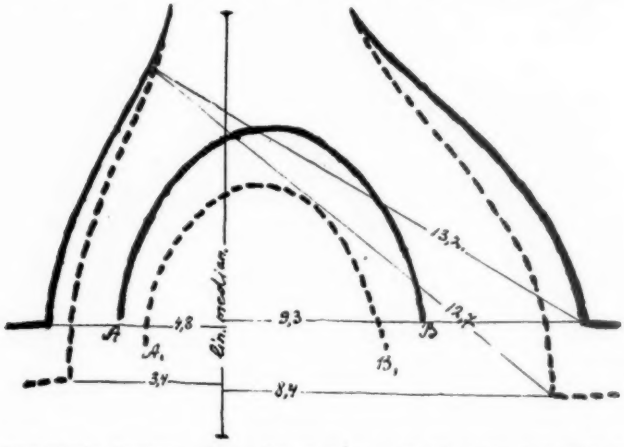

Fig. 1.—Hypotonic dystony of the heart in a man 25 years old with heart failure and dystrophic infantilism. (- - - -) The outline of relative and absolute cardial dullness with the patient at rest in the orthostatic (standing) position. (———) The same with the reflexes (change to clinostatic position, pressure on the eyeballs, fluoroscopy).

the diaphragm, one cannot get a fluoroscopic picture of the height of the diaphragm in the control state, and when the reflexes are already excited by the x-rays, it is only in cases of hyperexcitability of the vegetative nervous system that further reflexes can be elicited. For this reason one must rely on findings made out by percussion.

The determination of the left and right cardiophrenic angles is carried out during shallow breathing when, according to Hofbauer,[13] the central portion of the diaphragm, the heart and even the hilus of the lungs are not involved in the respiratory excursions. Determination of the position of the dome of the diaphragm by percussion is unreliable, and for our purposes percussion of both cardiophrenic angles is sufficient. The percussion is carried out finger-to-finger with quick strong taps as in defining the outline of relative cardiac dulness. We

checked the accuracy of this by comparing the contours determined by percussion under the influence of the x-ray reflex with the shadow on the screen, taking care to have the patient in the same position each time.

THE DIAPHRAGMATIC REFLEXES

In the case of healthy young persons with stable vegetative nervous systems, the tonotropic reflexes of the heart and diaphragm are either absent or insignificant, indicated by an excursion of not more than 0.5 cm. When present the reflex is always expressed as a lowering of the cardiophrenic angles, that is as an increase in the tone of the diaphragm.

We believe that this moderate hypertonic reflex, which occurs when the intragastric pressure is raised, is the normal protective reflex, an evidence of the immediate protective function of the diaphragm. Pressure on the eyeballs gives a reflex exactly similar to that caused by filling the stomach, even in cases where the rhythmic reflex of Dagnini-Aschner is absent.

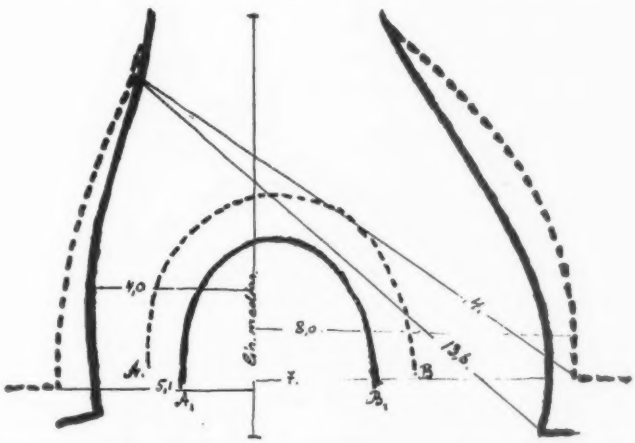

Fig. 2.—Dystony of the heart in a woman 25 years old with dystrophic infantilism. Outlines of the heart in clinostatic position, (_ _) before and (——) after pressure on the eyeballs.

This hypertonic tonotropic reflex of the diaphragm is often associated with a hypotonic tonotropic cardiac reflex (dilatation of the heart); that is to say, pressure on the eyeballs often increases the volume of the heart (negative tonotropic reflex) and at the same time lowers the diaphragm (positive reflex). This association is so frequent that we may assume that there is an antagonistic correlation between heart and diaphragm as well as between diaphragm and abdominal muscles.

This type of hypertonic reflex of the diaphragm is still more pronounced in persons with hyperexcitability of the parasympathetic system, especially in young persons with traits of dystrophic infantil-

ism. In such cases the changes already described as occurring in normal individuals are present but to a greater degree; the amplitude of the displacement of the cardiophrenic angles increases to 1 cm. or more, but the reflex still keeps its defensive character (Fig. 1). The most exaggerated type of reflex is seen in cases of spasmophilia and particularly in bronchial asthma.

The conditions change when the general picture becomes complicated by insufficiency of the diaphragmatic muscle followed by a high position of the diaphragm. As the dilated heart muscle can still respond to tonotropic reflexes of contraction or relaxation according to the state of the vegetative nervous system, so can the diaphragm which has lost its tone still maintain the protective type of tonotropic reflex. If there is a change in the relation between the heart and the diaphragm, particularly in cases of dilatation of the heart and permanent

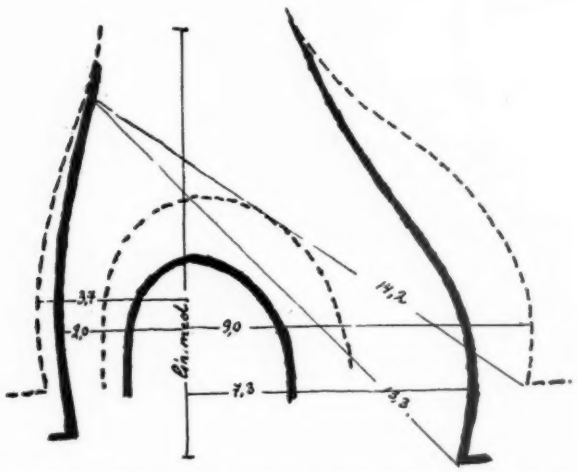

Fig. 3.—Hypertonic dystony of the heart in a man between 30 and 40 years old who had palpitation on exertion, (- - - -) at rest, (——) with the reflexes.

weakness of the tone of the diaphragmatic muscle, this defensive type of reflex may turn against those organs, principally the heart, which it has thus far protected. When there is functional insufficiency of the diaphragm in the presence of considerable cardiac enlargement, the heart pushes down the central portion of the diaphragm forming a deep depression, from the sides of which the two halves of the diaphragm rise quite abruptly. The hypertonic reflex of the diaphragm, increasing the tension of the latter, tends to decrease the inequalities of surface, lowering the domes and raising the central portion on which the heart rests. In other words, the hypertonic reflex is no longer purely defensive but has acquired an active aggressive character. This explains the complaints of patients who, having conserved the hypertonic diaphragmatic reflexes, suffer from aggravation of their symptoms—heaviness, breathlessness, palpitation—after eating, etc.

With loss of tone, however (diaphragma molle or relaxata), the diaphragm may take on an opposite type of reflex, may respond to stimuli by relaxation. The degree of loss of tone may vary according to the general state of the patient, especially according to the degree of fatigue. Altschul observed cases of relaxation of the diaphragm in which this was shown by the level of the domes being higher at night

Fig. 4.—Diagram illustrating relaxed diaphragm and enlarged heart.

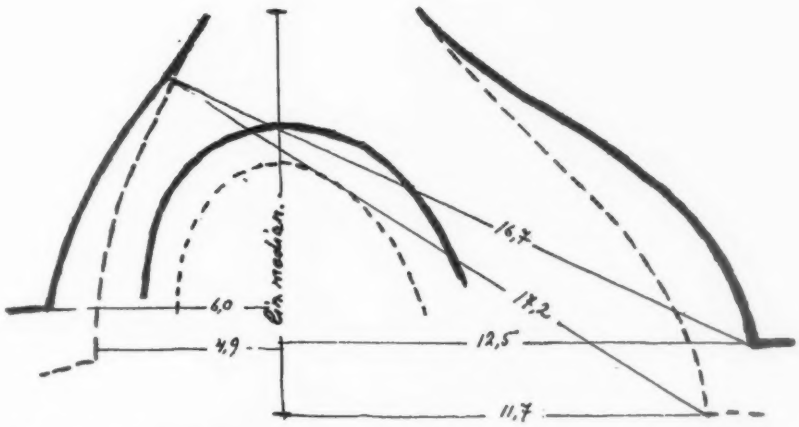

Fig. 5.—Cardiodiaphragmatic syndrome. Patient, a woman, 39 years old with dystrophia adiposo-hypogenitalis, heart failure, and sympatheticocrises affecting the heart, stomach and intestines. Outline of cardiac dullness with patient (- - - -) standing, and (———) sitting.

than in the morning. We do not know whether he considered the possibilities of various reflexes, such as filling the stomach.

As long as the diaphragm maintains its ability to counteract abdominal pressure, that of the stomach particularly, even considerable distention of the stomach does not affect the level of the diaphragm. Altschul,[14, 15] after x-ray studies, came to the conclusion that there was no definite relation between the height of the diaphragm and the degree of distention of the stomach. In another paper the same author

mentions a case in which filling the stomach or distending it with gas caused no displacement of the left hemidiaphragm.

When the muscle is hypotonic, one might expect that the decrease in intra-abdominal pressure resulting from the high position of the diaphragm and the relaxation of the abdominal wall would predispose to the accumulation of gas, would permit an increased amount of gas to collect in the stomach and intestine. In other words a collection of gas is not necessarily primary but may be secondary.

With decreased tone of the diaphragm, change in the autonomic balance in the direction of decreased excitability of the parasympathetic system, and the development of a whole series of sympathetico-tonic symptoms,* the protective function of the diaphragm is greatly disturbed.

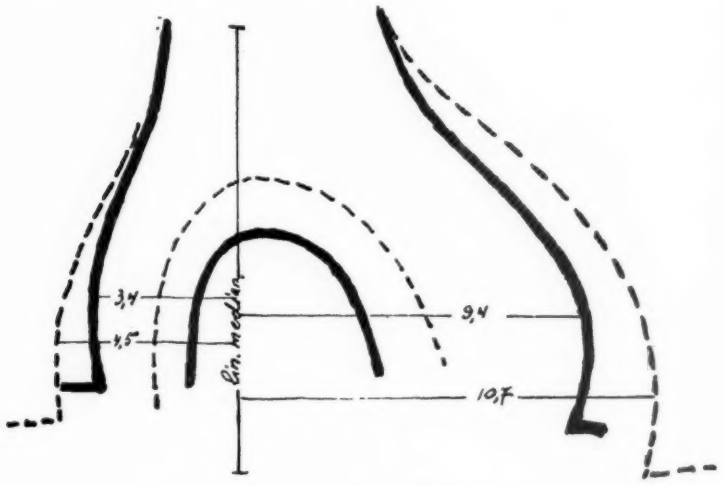

Fig. 6.—The effect of the injection of embryonal extract on the outline of the heart, (- - - -) control, (—) after injection.

Perversion of the function of the diaphragm alone ordinarily gives rise to no symptoms as long as the functions of the organs it protects are normal, as long as the heart is strong enough to overcome unfavorable conditions of work. According to Healy,[16] of 53 cases of relaxed diaphragm 47 were discovered accidentally by x-ray. But relaxation of the diaphragm followed by functional insufficiency of the organs which it normally protects, of the heart for example, is evident at once.

*We do not apply the term, "hypersympatheticotony" to the development of sympatheticotonic symptoms accompanying the ageing process, because we are not sure that the sympathetic system is not involved in this process, and that it is not subject to qualitative as well as to quantitative changes in its functions. Without disregarding the multiplicity of the functions of the sympathetic nervous system, we may remark that one function, trophic, is definitely disturbed as the organism grows old.

INSUFFICIENCY OF THE DIAPHRAGM

Insufficiency of the diaphragm with reference to its protective function can easily be determined by comparing its height with the patient standing and sitting. When the function is good, the level does not change perceptibly; but when it is insufficient, one gets another picture as is illustrated by the following case from the Out-Patient Department of the Polyclinic Tzekoubou.

A woman, 54 years old, was examined October 5, 1927. She presented evidence of dystrophia adiposogenitalis, had a relaxed flaccid abdomen, and complained of dyspnea and painful sense of distention of the upper part of the abdomen. She had not menstruated since an oophorectomy in 1908. The diaphragm was more than 2 cm. higher when the patient was sitting than when she was standing. From this it resulted that, in spite of the relaxation of the abdominal wall and the absence of increased abdominal pressure, the diaphragm and the abdominal press

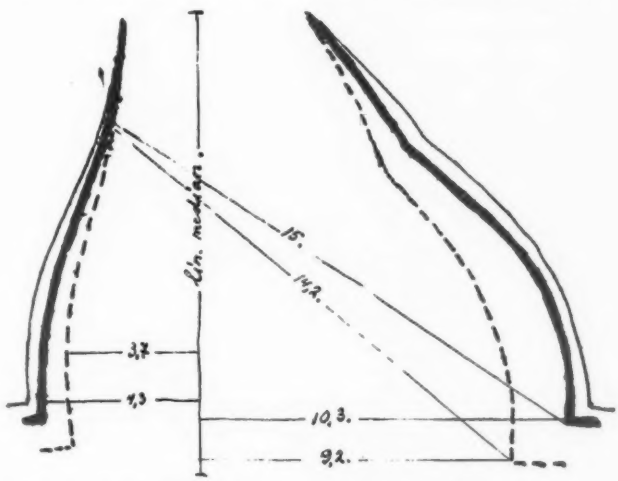

Fig. 7.—The effect of the injection of 1 c.c. of adrenalin, 1:1000; (——) control, (- - - - -) immediately after the injection, (——) 24 hours later.

having lost their protective function did not give physiological correlation between intra-abdominal and intrathoracic pressure and caused the development of a cardiodiaphragmatic syndrome. (For similar case see Fig. 5.)

Adipose dystrophy is not necessary for the development of the cardiodiaphragmatic syndrome. Patient K, for example (seen in office consultation) was a mechanic, 31 years old. He was thin. He had mitral stenosis which had followed an attack of acute rheumatic fever when he was 14 years old. Blood pressure was 134/84 mm., oscillometric index 12 m/n. He complained of dyspnea and palpitation after meals and particularly after heavy meals. Comparison of the level of the diaphragm with the patient sitting and standing showed that it was much higher in the former position.

Especially when patients with cardiac disease complain of malaise after meals, change of position, etc., we find more or less marked evidence of functional insufficiency of the diaphragm. The syndrome is the more serious when there is excitability of the visceral nervous

system. Nevertheless, the cardiodiaphragmatic syndrome, that is the development of a series of symptoms (palpitation, dyspnea, pain) due to elevation of the diaphragm resulting from its functional insufficiency (after eating or drinking, when sitting or lying down), is most frequently seen in persons with adipose dystrophy. It is most often seen in young persons with hypopituitary dystrophy and underdevelopment of the genitals (dystrophia adiposo-hypogenitalis), at the menopause or after oophorectomy, or in either sex with disturbance of the gonads. It is often associated with early sclerotic changes in various organs and a more or less marked functional insufficiency of the heart. Decreasing tone of the diaphragm, dilatation of the heart, deposit of abdominal fat, weakness of the abdominal muscles, and atony of the digestive tract are the factors which favor the appearance of the cardiodiaphragmatic syndrome. It is possible that distention and stretching of

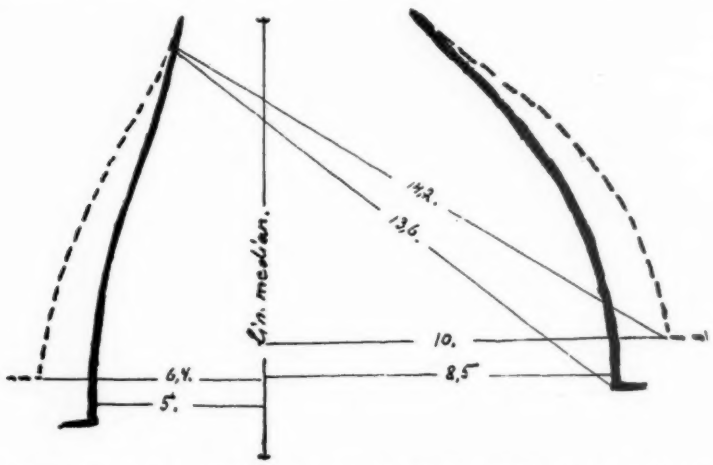

Fig. 8.—The effect of the injection of 1 c.c. of sodium nitrite, 10 per cent; (—) control, (- - - - -) after the injection.

the walls of the intestine may set up nervous stimuli affecting the heart and the diaphragm.

The experiments of Pearcy[17] are interesting in this connection. He showed that reflexes from the abdominal viscera (distended intestine, gall bladder or urinary bladder) had no effect on the hearts of healthy animals, but that a reflex was always demonstrable in cases in which a toxic myocarditis had been produced experimentally. Thus there is experimental evidence that the healthy heart is not markedly affected by stimuli from the abdominal organs, but that a diseased heart becomes the target for such stimuli.

One must assume that the heart, the diaphragm and every other organ may be influenced by pathological tonotropic reflexes from other organs under the following conditions, disturbance of the effector organ, hyperexcitability or unbalance of the visceral nervous system,

or functional disturbance of the receptor organ. In vagotonic cases these tonotropic reflexes are expressed as dilatation of the heart and increased tone of the diaphragm, but in such cases the rôle of the diaphragm is of minor importance. In sympatheticotonic cases the tone of the heart is increased while that of the diaphragm is decreased, giving rise to the discomfort of the so-called sympatheticotonic cardiodiaphragmatic syndrome, in which the cardiac symptoms are prominent and the rôle of the diaphragm is essential.

From this description of the syndrome we omit to mention the respiratory disturbances, for these probably bear no immediate relation but are produced by circulatory and anoxemic disturbances of the respiratory center. Indeed, there may be disturbances of other organs in this cardio-abdomino-diaphragmatic syndrome, but the factors of the heart, the diaphragm, the abdominal press, and the nerve tonus are of fundamental importance. In diagnosing and interpreting the mechanism of the syndrome none of these factors should be considered alone, for only by taking all together can the syndrome be understood.

TREATMENT OF THE CARDIO-ABDOMINO-DIAPHRAGMATIC SYNDROME

While symptomatic treatment may give satisfactory results, it is only by considering more broadly the mechanism of the syndrome that we can determine the possibilities of rational treatment.

In recent years we have found that in cases of cardiodiaphragmatic and abdominovisceral syndrome based on dystrophia-adiposo-hypogenitalis good results may be obtained from the injection of 1 c.c. of pituitrin, two, three or four times weekly, combined with daily injection of glandular extracts depending on the sex of the patient (ovarian, testicular, spermine, etc.). At times, when the picture is complicated by hypothyroidism, we give thyroid extract by mouth once or twice daily, regulating the dose by the indications of the individual case. While there can never be a complete restoration of the normal state, in the entire series of cases symptomatic improvement was the rule. Attacks caused by the condition became milder and less frequent or disappeared completely; the function of the intestines improved and gaseous distention disappeared; the diaphragm became lower; and what is specially characteristic, the painful symptoms of adiposa dolorosa became milder and disappeared. (This is particularly true of women at the menopause.) Among other cases I can cite that of a singer who under this treatment lost 15 pounds, regained the normal function of her diaphragm and was able to move about freely without dyspnea. I have a series of women over fifty years old, who under this treatment lost their discomfort after eating and regained their ability to sleep flat in bed and to lead active lives. One patient, whom

I have observed for almost two years, has even ceased to have anginal attacks.

We have made a number of experiments to determine the possibility of securing a prompt and vigorous effect on the tone of the diaphragm. While strychnine and extracts of the sexual glands have a definite action in such cases, this action develops so slowly that it is difficult to study it experimentally after a single dose.

A single injection of adrenalin, pituitrin or embryonal extract produces a definite effect on the tone of the diaphragm. This is best seen in cases in which there is not great increase in the size of the abdominal cavity, in which the diaphragm is not fixed and in which the abdominal muscles retain their power.

Fig. 6 represents the effect of a single subcutaneous injection of 1 c.c. of embryonal extract in a patient with infantile dystrophy and a high position of the left dome of the diaphragm. After this injection the two cardiophrenic angles were lowered. The following two or three injections served to establish the new level of the diaphragm and to abolish the hyperactivity of its reflexes.

It is true that when the heart is dilated and pressing down upon the central portion of the diaphragm a decrease in the volume of the heart decreases this pressure of the heart on the diaphragm, and an injection of embryonal extract may produce a paradoxical result. For example, the cardiophrenic angles may rise, as we see in Fig. 4 of our paper "The Effect of Embryonal Extracts on the Tone of the Heart Muscle in Cases of Infantilism." Fig. 1 of the same paper shows a similar effect from a subcutaneous injection of 1 c.c. of a 1:1000 solution of adrenalin.

The effect of embryonal extract lasts from twenty-four to forty-eight hours, or even longer, but the effect of adrenalin disappears within from eight to twelve hours, and within twenty-four hours the diaphragm has returned to its original level or is in an even more unfavorable position. Pituitrin is less active than embryonal extract, but its effect lasts longer than does that of adrenalin, and after its use there is never the marked decrease in tone which may be observed after adrenalin.

Sodium nitrite lowers the tone of the diaphragm. It produces dilatation of the heart and decreases the spastic tonotropic reflexes.

Fig. 8 indicates the response to the injection of 1 c.c. of a 10 per cent solution of sodium nitrite. The patient was a laborer, 38 years old, with moderate hypertension, blood pressure 156/90 mm., but without arteriosclerosis. He complained of pricking precordial pain, sense of oppression, dyspnea, and anxiety after fatigue, after meals, when excited, and at night. Subjectively there was considerable relief after the first subcutaneous injection of sodium nitrite, but with this the heart was dilated, both cardiophrenic angles were elevated, and there was no objective evidence

of improvement. Apparently the subjective improvement was produced by the change in the vegetative nervous tone of the heart resulting in dilatation and lessened response to reflexes.

With embryonal extract, pituitrin and extracts of the gonads, we improve the whole condition, but with sodium nitrite we only remove the spastic heart symptoms. It may be useful to remove these symptoms, but we believe the other treatment to be more useful.

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Department of Clinical Reports

TOXIC MANIFESTATIONS OF BARIUM CHLORIDE IN A PATIENT WITH COMPLETE HEART-BLOCK*

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IN RECENT years, the administration of barium chloride has been advocated for the prevention of syncopal attacks associated with standstill of the ventricles in patients with complete heart-block.[1] The basis for the use of this drug depends upon its ability to keep the idioventricular pacemaker in an irritable state and thus prevent ventricular standstill, which in the majority of these cases is responsible for periods of unconsciousness that accompany this type of inactivity of the heart.

The exact dosage of the drug needed to produce the desired effect is still unknown. According to Levine[2] it is probably 30 mg. four times a day, while Herrmann and Ashman[3] have reported "spectacular" results without any detrimental effects from the use of heavy doses over prolonged periods of time. Indeed, in one of their patients the oral administration of a single dose of 20 grains (given by mistake) produced no untoward symptoms save nausea and vomiting and a moderate diarrhea.

The following patient with complete heart-block is of particular interest because after the administration of only 60 mg. of barium chloride, he showed within several hours an irregular acceleration of the ventricles with alarming symptoms of extreme breathlessness and signs of circulatory collapse, all of which cleared up with the elimination of the drug.

REPORT OF CASE†

L. R., male, aged fifty years, a tailor, was admitted to the Montefiore Hospital on August 5, 1927 and died on November 28, 1927. He was suffering from heart failure and complete heart-block and from the time of his admission to the wards he became progressively worse. He was dyspneic and cyanotic; his legs were markedly swollen, and he showed hydrothorax and ascites. In the last few months of his illness he responded very poorly to graded doses of digitalis. Following the administration of approximately 50 c.c. of tincture of digitalis within one week, during a time when he was known to show complete heart-block with a ventricular

*From the Medical Division of the Montefiore Hospital for Chronic Diseases, New York City.

†This case was reported in detail in connection with another phase of therapy, so that only its salient features are given here. *Vide*, The action of Digitalis in Complete Heart-Block, The Am. Heart J. (to be published).

rate of 41 and an auricular rate of 68 beats per minute, the patient developed an irregular acceleration of the ventricles averaging 98 beats per minute, with bigeminal rhythm and auricular fibrillation. These abnormal rhythms were considered toxic manifestations of digitalis and all of them disappeared so that three weeks later there was again complete heart-block with a regular ventricular rate of 41 beats per minuts and an auricular rate averaging 88. (Fig. 1.)

At this time, October 23, 1927 at 9 A.M. when his heart rate was regular, the patient was given two doses of barium chloride of 30 mg. each within four hours.

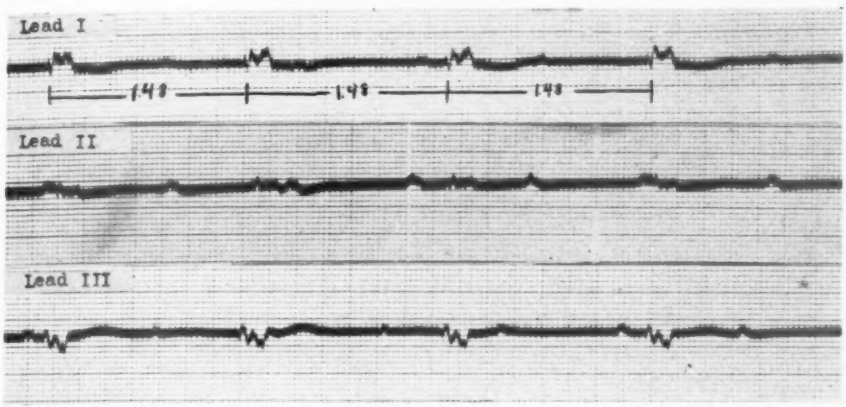

Fig. 1.—Ecg. No. 2844. Complete heart-block before the administration of barium chloride. Ventricular rate 41, auricular rate 88. Note also the intraventricular conduction disturbance (arborization block) i.e., low voltage and prolongation with deep notching of the QRS complexes.

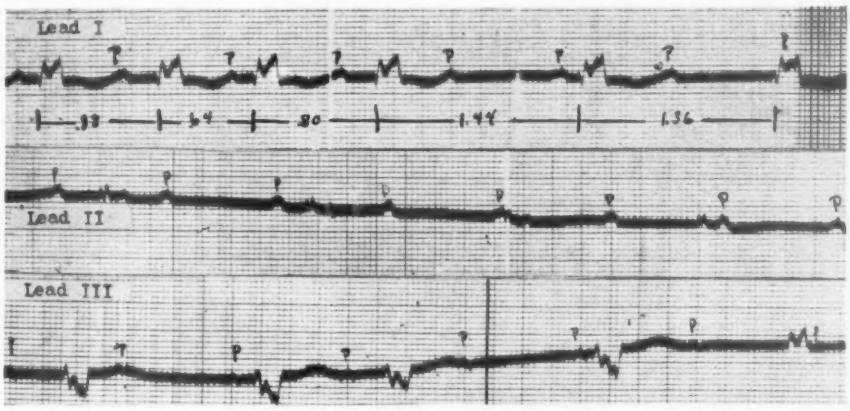

Fig. 2.—Ecg. No. 2974. After the administration of barium chloride. Irregular acceleration of the ventricles. The auricles are not affected.

His general condition preceding this was poor, but he was breathing with ease and he was not cyanotic. His legs were extremely swollen; he showed no signs of fluid in his chest, and there was only moderate ascites.

Following the administration of the last dose of barium chloride, the patient's condition became suddenly worse. He breathed with difficulty and his respirations were irregular. His face became intensely cyanotic and his sensorium was very disturbed. He was disoriented and his speech became unintelligible. For the next

hour it was difficult to arouse him and severe pressure over the supra-orbital nerve just caused him to groan. Large beads of perspiration appeared on his forehead. His pulse was barely perceptible.

Coincidentally with these changes in his symptoms there was noted a very marked irregularity of his heart rate. This was now totally irregular and although there was no pulse deficit, even to the trained observer the rhythm resembled that of auricular fibrillation with an irregular ventricular rate which at times was as high as 93 beats per minute. The electrocardiograms taken at this time showed an irregular ventricular acceleration due to stimulation of the idioventricular pacemaker. The auricles were not affected by this change. (Fig. 2.)

The irregularity of the heart disappeared toward the evening of this day and with the restoration of the dominant rhythm of complete heart-block the patient began to feel much better.

It was impossible to repeat this test, as the patient refused to take any more medication. He died on November 28, 1927 and during the rest of the period of observation, he never showed any irregularities except a complete heart-block.

COMMENT

While, as experience has shown, barium chloride may be a safe drug to prescribe to patients with complete heart-block suffering from Stokes-Adams disease, there is probably a group of cases with auriculoventricular dissociation in which the drug produces deleterious effects. It is possible that these patients who are so susceptible to the drug, as in the case reported here, may never show the signs of ventricular standstill and that the response to barium chloride represents in them a highly irritable idioventricular pacemaker. Nevertheless it is important to realize that it does not require much of the barium chloride to produce toxic symptoms in an individual susceptible to the drug. For this reason attention is called to the fact that caution and care must be exercised in the administration of barium chloride to any patient with heart-block.

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A CASE OF PAROXYSMAL TACHYCARDIA IN THE COURSE OF ACTIVE SUBACUTE BACTERIAL ENDOCARDITIS*

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CASE REPORT

C. K., male, 23 years old, was admitted January 11, 1929, complaining of fever, cough, and pain in the right side of the head. The onset of the illness occurred two months before admission, with a cold accompanied by cough and blood-streaked sputum. One week before admission the patient began to feel feverish, had night sweats and developed pain in the right side of the head, left shoulder and left foot.

Family History.—Essentially negative.

Previous History.—Pleurisy and pneumonia four years before. No history of tonsillitis, rheumatic fever or chorea. No history of gonorrhea.

Physical Examination.—The patient was a young adult male, well developed, presenting marked pallor, not exactly of the café au lait type. The conjunctivae showed no petechiae; the ocular conjunctiva was pearly; pupils were equal and reacted to light and in accommodation; eyegrounds negative. Nose was clear; pharynx was slightly injected. No adenopathy. There was slight tenderness at the left subacromial region and at the left ankle. Lungs: slightly impaired resonance at the right apex and left base; no râles. Heart: some increase in the horizontal diameter, especially to the left; presystolic and systolic murmurs at apex with synchronous thrills; the systolic murmur was transmitted posteriorly and was heard down to the second lumbar vertebra; short, coarse, diastolic murmur at the base. Blood pressure 100/70 mm. Spleen: just palpable; slight left para-umbilical tenderness. Liver not palpable. Knee jerks present and active.

Diagnosis on Admission.—(a) Chronic rheumatic cardiovascular disease; (b) mitral stenosis and insufficiency; (c) mitral and aortic valvulitis; (d) subacute bacterial endocarditis.

Subsequent Course.—January 13. Osler node noted on middle finger of left hand.

January 14. Blood culture negative.

January 15. Patient fell and was found to have a left arm paresis and a left supranuclear facial paresis. A petechia was noted in the upper right lid; eyegrounds negative.

January 18. Paroxysmal tachycardia noted, rate 190. Patient complained as usual of pain in right temporal and facial regions and in left loin.

January 20. Paroxysmal tachycardia continued. Patient did not complain of his cardiac condition.

January 21. Left hemiparesis; Babinski sign, positive; ankle clonus present; no petechiae observed. Patient did not complain of his paresis or cardiac arrhythmia. Still distressed about facial and loin pain. EKG paroxysmal tachycardia, rate 188, auricular.

*My thanks are due Dr. Alexander Lambert, Director of the Fourth Medical Division, and Dr. Douglas Symmers, Director of Laboratories, Bellevue Hospital, for permission to report this case from the wards of Bellevue Hospital.

Read before the New York Pathological Society, March 14, 1929.

January 23. Heart rate as before; no subjective or objective evidences of decompensation.

January 24. Rate down. Patient conscious of change of heart rate but unconcerned. Slight neck rigidity; no Kernig.

January 26. Phlebitis of vena mediana cubiti.

January 31. Blood culture positive for Streptococcus viridans after 144 hours. A single white centered petechia noted on right wrist.

February 6. Pustules on left buttock.

February 19. Pain in left loin exacerbated. Diagnosed as infarct of kidney or perisplenitis. No red blood cells found in urine.

February 20. Few râles noted in left axilla.

February 28. Patient vomited early in morning; soon went into coma. Spasticity developed in upper and lower extremities. Right pupil larger than left. Cheyne-Stokes breathing followed.

March 1. Patient died at 4:05 A.M.

During the course of the illness the temperature averaged 102° F. with many fluctuations. The patient received digitalis, aspirin, codein, and occasionally hypnotics.

Post-mortem Examination.—Only positive findings are given. Numerous petechiae of conjunctivae; several petechiae over right shoulder posteriorly; multitudes of petechiae over right and left pleurae. Left hemohydrothorax (over 1000 c.c.). About 300 c.c. of serous fluid in pericardial sac; weight of heart 350 gm. Several petechiae were present in the wall of the right auricle. The mitral valve showed some stenosis. There were verrucous vegetations of this valve, extending to the chordae tendineae and well upwards on the auricular wall. At the cephalic pole of the limbus fossae ovalis there was dusky discoloration of the endocardium, which upon cut section seemed to be a small ecchymosis. One of the leaflets of the aortic valve presented a sessile, flat vegetation from 3 mm. to 5 mm. in diameter. Another of the leaflets showed a large petechia. The liver weighed 1950 gm.; on cut section it was dark red. The spleen was somewhat large, weighing 260 gm., and showed two large infarcts of different age. Both kidneys together weighed 300 gm. The capsules stripped with difficulty, and the surface was somewhat granular; the left kidney showed no other gross abnormality; in the right kidney were numerous infarcts. The brain was not examined. The myocardial petechiae were confirmed by histological study. In the ventricular myocardium there was one large focal accumulation of large mononuclear cells; there were scattered foci of fibrotic change, especially in the myocardium beneath the mural endocarditis.

DISCUSSION

The view commonly held of the infrequency of cardiac arrhythmias in subacute bacterial endocarditis and the pertinent one of an infrequency of myocardial involvement are well expressed by Bickel:[1] "It is remarkable that functional alterations of the excito-conduction system, so frequent in the most diverse general toxi-infections, have been noticed only exceptionally in diseases predominantly localized to the endocardium, such as the septic endocarditides. They seem particularly rare in 'l'endocardite à évolution lente,' and we have not been able to encounter a single case in a rapid bibliographical study." This accords well with the fact noticed by most authors of the rarity of myocardial involvement. Debré tells us in his excellent general review: "The myocardium is slightly involved, the pericar-

dium is intact, besides patients complain little of their hearts and the functional disturbances are inconstant and reduced to a minimum."

Homer Swift[2] says, "Instrumental signs of extensive parenchymatous irritation of the heart are as rare in subacute bacterial endocarditis as are peripheral signs of exudation." Bickel describes a case with heart-block. The only other case with an arrhythmia definitely diagnosed as active subacute bacterial endocarditis that I have been able to find is one of auricular fibrillation reported by Rothschild, Sacks and Libman.[3]

THE MYOCARDIUM

Blumer[4] in a study of 150 cases of subacute bacterial endocarditis found chronic interstitial involvement of the myocardium in 5 per cent (8 cases) and acute myocarditis in a little over 1 per cent (2 cases). Clawson[5] found inflammatory myocardial changes in 24 per cent of 54 cases of subacute bacterial endocarditis. Thayer[6] in a more intensive study found acute myocardial involvement in 60.8 per cent and chronic fibrotic changes in 63.6 per cent of his cases. Considering the generally accepted view of the precedence of subacute bacterial endocarditis by rheumatic fever in which myocardial involvement is "invariable," one should expect a proximate frequency of at least the fibrotic change in subacute bacterial endocarditis. As for the acute inflammatory change, the truth might well be approached by an application of Mackenzie's[7] general dicta: "Another point to bear in mind is that in the invasion of the heart the specific organism rarely affects one tissue alone. In order to be exact and methodical writers usually describe separately the symptoms of endocarditis, myocarditis and pericarditis. But if one reflects on the nature of the symptoms, such as the condition of the pulse, its strength and rate, the size of the heart and the precordial distress—the symptoms which are usually included in the description of endocarditis and pericarditis—it will be realized that they are not really the manifestations of endocarditis or pericarditis but are the signs of a myocardial affection."

The discrepancies in the studies cited and the difference between apparent fact and so valid a supposition as Mackenzie's are strange. From the point of view of diagnosis, prognosis and a better clinical and pathological understanding of the disease, it is essential that these opposing views be correctly estimated. The symptoms, clinical features and pathological findings, each offers a barrier to our knowledge of myocardial involvement in subacute bacterial endocarditis. Clinically, as Debré[8,9] accurately states, "These patients are cachectics, never cardiacs." It is well to remember, however, that peripheral congestive phenomena are not the only evidences of cardiac decompensation. Clinically, also, the anemia and peripheral embolic phe-

nomena are so striking and varied that they attract almost the entire attention of the clinician. This is quite different from the monotonous regularity of the congestive phenomena of chronic cardiovalvular disease where the cardiac signs and close digitalis control become so engaging. Pathologically, the endocardial involvement so obtrudes that we are apt to and really do neglect a more careful study of the myocardium. It is quite probable that when we have pursued our studies of the living and dead myocardium in subacute bacterial endocarditis with the persistence with which we have pursued the presystolic murmur and the Aschoff body in acute rheumatic fever, we shall find little if any percentage disparity of myocardial involvement in these two diseases. The report of this case is a small effort in that field.

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Department of Reviews and Abstracts

Selected Abstracts

Cutler, Elliott C. and Beck, Claude S.: The Present Status of the Surgical Procedures in Chronic Valvular Disease of the Heart. Arch. of Surg. **18**: 403, 1929.

This article summarizes the twelve cases of chronic valvular disease of the heart that have been subjected to operation. The cases included one of pulmonic stenosis, one of aortic stenosis and ten cases of mitral stenosis. Of the ten patients with mitral stenosis who were operated upon, one only is living, a mortality of 90 per cent. Eight of the ten patients died so soon after the operation that the changes brought about in the mechanics of the circulation could not be adequately studied. One patient lived four and one-half years after the operation.

There have been three kinds of procedures utilized in the attempts to enlarge the stenotic orifice. These methods are finger dilatation, incision of the stenotic valve and excision of a segment of the stenotic valve.

The authors feel that the twelve cases are not sufficiently numerous to justify conclusions as to the value of the operation nor is it possible to answer certain questions that arise in this connection. The mortality figures alone should not deter further investigation both clinical and experimental.

Ochsner, Alton and Herrmann, George R.: Experimental Surgical Relief of Experimentally Produced Pericardial Adhesions. Arch. of Surg. **18**: 365, 1929.

The authors have studied in 65 dogs the question of the removal of pericardial adhesions after the subsidence of the acute symptoms of acute pericarditis produced experimentally. In one group of animals a digestant was introduced in order to prevent the reformation of adhesions after the second operation. In another group of control animals physiologic sodium chloride was introduced into the pericardial cavity. In the third group merely the division of the adhesions was performed. In these groups with or without the introduction of saline solution, adhesions invariably reformed.

In three of the ten dogs treated by digital separation of the adhesions with the introduction of a digestant solution into the pericardial cavity no adhesions reformed. The remaining seven animals showed evidence of extensive pleural infection.

As the result of the study on these animals, the authors conclude that intrapericardial as well as extrapericardial adhesions are significant and produce cardiac embarrassment. The two types of adhesions are usually associated. They discuss the value of surgical intervention during the acute stage of purulent pericarditis in order to establish external drainage. They believe that further perfection of technic will enable them to introduce a vegetable digestant (not described in this article) into the pericardial cavity in order to prevent the reformation of adhesions following an operation devised to break these adhesions up.

Lockwood, Ambrose L.: Surgery of the Pericardium and Heart. Arch. of Surg. **18**: 417, 1929.

In this article the author reviews the literature relating to this subject and discusses the various surgical procedures that have been devised to relieve injuries and disease of the heart. Among the important points to be learned from such a

study, the following may be mentioned. If the patient has lost much blood with a lowered arterial tension, the wound in the heart may temporarily cease to bleed, whereas when the patient's condition improves and the blood pressure rises delayed primary hemorrhage may occur and the patient may be found "in extremis." Injury of the bundle of His is often fatal. Pressure on the bundle of His or kinking and rotation of the heart by interfering with conduction through the bundle of His in doing the cardiorraphy may cause the heart to fibrillate or arrest entirely. Wounds of the heart heal by the formation of a cicatricial scar, not by true regeneration of muscle. Spontaneous eruption of the scar has frequently occurred following strain.

He also points out that a supporting stay suture through the apex is most valuable if elevation or rotation of the heart is necessary. Gauze should not be employed within the pericardium. Sterile water only should be employed to cleanse the pericardium. No antiseptics should be employed to the serous surfaces.

Great care must be taken to avoid infection bearing constantly in mind that most of the deaths after twenty-four hours have been due to infection.

He concludes that cardiolysis in selected cases should be more commonly practiced. Cardiorrhaphy for injuries of the heart should be promptly undertaken when indicated, especially if hemorrhage is occurring.

Sutherland, G. A. and McMichael, John: The Pulse Rate and Range in Health and Disease During Childhood. Quart. Jour. Med. **22**: 519, 1929.

The authors have noted that there is a normal variation in the heart rate of children between that of the sleeping and that of the waking hours amounting to more than thirty beats. This nocturnal slowing is probably of great importance for the child. Sleep for the child thus becomes a means of rest not only to the body but to the heart also. The authors believe that the explanation of the extreme variability of the pulse rate in childhood lies in the unstable nervous system of the child. They point out that the "normal" heart rate is present only when the child is asleep and when the unstable central nervous mechanism which controls the vagus and sympathetic nerves is free from disturbance of all outside stimuli. When the child goes to sleep, some time elapses before the effects of the stimulation of the nervous system during the waking hours pass off, the lowest level being reached between midnight and four A.M. They have also observed that when the child falls asleep in the early afternoon the pulse rate falls though usually not quite so low as the minimum nocturnal rate.

In studying a group of children with rheumatic carditis they have noted the pulse rate continues rapid day and night and cannot be slowed or altered by any amount of rest. This rapid pulse may be the only sign of activity in a case of rheumatic carditis. They feel that this is a useful sign to be noted in the care of children with carditis.

Derick, C. L. and Hitchcock, C. H.: An Address on the Allergic Conception of Rheumatic Fever. Canad. Med. Assoc. J. **20**: 349, 1929.

In this address the authors review the literature and their own work on rheumatic fever which has brought about the conception that this disease may be of an allergic nature. They point out the similarity between this disease and tuberculosis and the development of hypersensitivity to tuberculous infection.

Much of the recent work done on streptococcus infections and on rheumatic fever in particular indicate the existence in certain individuals of a condition of hypersensitiveness to streptococci resulting from repeated low-grade infections or from the persistence of foci of infection in the body.

When under suitable circumstances, streptococci or products of streptococci are disseminated to the tissues, these tissues overact and the character picture of the disease results. When on the other hand there exists a condition of immunity or of normality in contradistinction to this peculiar hypersensitive state, the dissemination of streptococci results in a minimum of injury to the tissues and the characteristic phenomena of the disease fail to appear.

Kaiser, Albert D.: The Relation of the Tonsils to Acute Rheumatism During Childhood. Am. J. Dis. Child. **37**: 559, 1929.

In this survey 439 children who had acute rheumatism were studied and a special effort was made to determine the relationship of the rheumatic attacks to the presence or absence of the tonsils. Cases of chorea or rheumatic endocarditis were not included in the study unless there had been evidence of involvement of joints or muscles. Efforts have been made to answer the following questions in this study. Does acute rheumatism develop for the first time as frequently in children whose tonsils have been removed as in those not operated on? Nearly twice as many children in the community studied developed the first attack of rheumatism when the tonsils were still present. This marked difference in the incidence of the disease suggests that the presence of tonsils predisposes to the first attack of acute rheumatism and conversely that the removal of the tonsils offers considerable hope of escape from this infection. Two, Do recurrent attacks occur as often in children whose tonsils have been removed after one attack of rheumatism as when the tonsillectomy has not been performed? Recurrent attacks of rheumatism occur 10 per cent less often in children who had their tonsils removed after the first attack of rheumatism than in those whose tonsils were not removed. Three, Do recurrent attacks occur as often in children who have their first attack after the tonsils have been removed? The figures indicate that rheumatism developing for the first time in a child who has had the tonsils removed is more likely to recur than in the patient who is infected before tonsillectomy. Four, Does endocarditis occur as frequently in children who had acute rheumatism following a tonsillectomy as when the tonsils have not been removed? The incidence of carditis in the group of children studied is as high in one group who have had tonsillectomy as in those who have not.

Derick, C. L. and Swift, Homer F.: Reactions of Rabbits to Non-Hemolytic Streptococci. 1. General Tuberculin-Like Hypersensitiveness, Allergy, or Hyperergy Following the Secondary Reactions. J. Exper. Med. **44**: No. 4, 615, 1929.

In previous communications the authors have reported the phenomenon of secondary reaction to certain strains of green streptococci. Briefly this consists of an inflammatory reaction which appears about the 8th to 10th day after intracutaneous inoculation of rabbits with these microorganisms and at a time after the primary reaction has receded.

The object of this present communication is to present the detailed evidence which indicates that after the development of the secondary reaction animals have a type of hypersensitiveness which closely resembles so-called tuberculin allergy. This state is made evident by increased reactivity of the skin to reinoculation with small doses of these streptococci, by the marked reactivity of the scarified cornea to instillation of the streptococci into the conjunctival sac and by the death of many of the animals following intravenous inoculation with cultures in amounts well tolerated by normal rabbits. The lesions found in the lymphatic and hematopoietic organs of these animals are grossly very similar to those described originally by Koch in tuberculous animals following inoculations

with large doses of tuberculin. The authors have observed similar lesions in normal rabbits following intravenous injections of the more virulent hemolytic streptococci and have noted ophthalmic reactions similar to those seen in hypersensitive rabbits following primary inoculations of the cornea of normal rabbits with living hemolytic streptococci. Thus the condition of the hypersensitive rabbit has been altered in such a manner that the relatively avirulent nonhemolytic streptococci set up immediate reactions grossly comparable to those which follow infection of normal animals with virulent hemolytic streptococci.

The evidence brought out in this study shows that foci some place in the body are necessary for the development of this type of allergy because hypersensitiveness did not follow intravenous inoculation. Rapid destruction of the microorganisms without the production of large focal lesions probably offer a suitable explanation of this phenomenon.

The authors believe that following the intracutaneous inoculation of rabbits with any strain of streptococcus there develops a state of tuberculin-like hypersensitiveness but certain strains possess the capacity of stimulating the hypersensitiveness to a higher level than others and certain rabbits are more capable of reacting as is made evident by retesting the animals in different ways. Following the primary intradermal reaction there persists at this primary focus a certain amount of residual antigenic substance. When a sufficiently high degree of general hypersensitiveness develops, the cells in the immediate vicinity of the primary lesion are in a condition to react with small amounts of suitable bacterial substances whether they are either freshly introduced or residual. The secondary reaction is, therefore, apparently an evidence of this reaction with some residual antigen persisting at the site of primary inoculation in an animal which has developed a general state of hypersensitiveness. The peculiar feature is that some strains should possess these stimulating or reacting substances to such a degree, while others are strains apparently lacking in them.

Swift, Homer F. and Derick, C. L.: Reactions of Rabbits to Non-Hemolytic Streptococci. II. Skin Reactions in Intravenously Immunized Animals. J. Exper. Med. **44**: No. 5, 883, 1929.

In previous papers it has been shown that rabbits inoculated in practically any manner except intravenously with sufficiently large doses of certain nonhemolytic streptococci develop a condition of tissue hypersensitiveness whereas if the primary inoculation of the animal had been by the intravenous route using amounts of culture and time intervals comparable with those employed in the hypersensitized rabbits these intravenously inoculated animals responded with none of these reactions of hypersensitiveness. The present paper presents evidence that these intravenously inoculated rabbits react differently than do normals or hypersensitive rabbits to intracutaneous inoculation.

These subsequent intracutaneous inoculations with homologous streptococci produce reactions with smaller and harder lesions than are shown by normal animals and they do not develop the general manifestations of hypersensitiveness such as are shown by animals previously inoculated into the tissues with the same cultures. The lesions have little or no edema and are hard and firm after 24 to 48 hours. These lesions show much less change in size after two hours than do the lesions in other types of animals. This reaction has been described by the authors as an immune type of reaction.

They also have noted that certain rabbits give reactions following intracutaneous inoculation which are soft, have very little color, fade rapidly and do not show secondary reactions. They occur in rabbits which appear sick either due to an overwhelming reaction from streptococci or from any other cause. They have

designated these reactions as cachectic and are seen in animals with a negative state of anergy. This type of reaction is in contrast to the hypersensitive animals who react secondarily with signs of redness and swelling. This type of reaction indicates a positive state of hyperergy.

Birkhaug, Konrad E.: Rheumatic Fever. J. Infect. Dis. **44**: 363, 1929.

A series of 3,114 skin tests was performed during the summer of 1928 in European clinics on 594 individuals among whom were 42 active and 146 inactive or cured cases of rheumatic fever, carditis and chorea, 69 cases of chronic arthritis and degenerative arthritis and 33 per cent nonrheumatic controls. Excessive universal hypersensitiveness was found among 68 per cent of all types of acute rheumatic fever infection, to the filtrates or autolysates and bacterial suspensions produced by the hemolytic streptococcus.

Hypersensitiveness to nonhemolytic streptococcal products is most marked among active cases of rheumatic infection. Only 33 per cent of active and 29 per cent of inactive rheumatic fever individuals react to hemolytic streptococcal products, while 25 per cent of nonrheumatic controls react to the hemolytic and 14 per cent to the nonhemolytic streptococcal products. Among a series of 69 cases of chronic arthritis, 53 were due to infectious processes and 47 per cent of these react markedly to the products of both nonhemolytic and hemolytic streptococci.

Nye, Robert N. and Seegal, David: Non-Hemolytic Streptococci and Acute Rheumatic Fever. J. Exper. Med. **44**: No. 4, 539, 1929.

Blood cultures have been taken from 25 available cases of acute rheumatic fever according to the methods of Clawsen, Small and Birkhaug. These cultures were negative for nonhemolytic streptococci of both the alpha and gamma types. Nonhemolytic streptococci were frequently recovered from the throats of patients with this disease as well as from the throats of normal individuals.

Although these nonhemolytic streptococci were morphologically and culturally identical not only amongst themselves but also when compared with stock Small and Birkhaug strains, all including the latter have failed to show any noteworthy degree of homogeneity.

Representative strains of these streptococci have proved to be relatively nonpathogenic for rabbits following intravenous injection.

Hanzlik, P. J.: A New Method of Estimating the Potency of Digitalis: Pigeon-Emesis. J. Pharm. and Exper. Therapeu. **35**: 363, 1929.

The author proposes a method for estimating the potency of digitalis directed toward the evaluation of a probable therapeutic dosage by determining the maximum emetic dose in pigeons.

Adult pigeons of from 300 to 400 grams body weight are used. The estimated dose of the digitalis preparation is injected into a suitable wing vein in the axillary region of the bird. On completion of the injection the pigeon is replaced into a cage for observation of vomiting which is recognized by downward craning movements of the head and usually flapping of the wings with occasional expulsion of gravel. These symptoms are generally preceded by symptoms of nausea, that is, swallowing due to increased salivation, lacrimation and ruffling of feathers of the head and neck. Vomiting occurs in from three to ten minutes depending on the dosage of the preparation used. In determining the minimum emetic dose a series of pigeons is injected and the just effective dose causing emesis in two out of three pigeons is noted.

The method has been compared with the official frog method and the cat method and a number of factors effecting the accuracy and application of the pigeon method have been considered. The method is simple, easy, convenient, economical and reasonably accurate. The minimum emetic dose of digitalis causes changes in the pigeon heart which are characteristic of advanced digitalis action thus further justifying expectations of therapeutic action when this dose per kg. in pigeons is transferred directly and given by mouth to man.

Hanzlik, P. J., and Stockton, A. B.: Results with the Pigeon-Emesis Method of Estimating the Probable Therapeutic Dose of Digitalis. J. Pharm. and Exper. Therap. **35**: 393, 1929.

The circulatory and side actions of tinctures of digitalis, assayed by the pigeon-emesis method were observed in six convalescent and two pathological human subjects who received the preparations by mouth. The effects were controlled in three subjects receiving alcohol and atropine.

Fully developed actions of digitalis were produced in the majority of the subjects as indicated by sustained slowing of the pulse, fall of blood pressure and reduced pulse pressure, the doses agreeing closely with the probable doses estimated from the minimum emetic doses in pigeons.

Nausea and emesis occurred in one-half the subjects receiving the digitalis thus corroborating the high efficiency of the clinical dosage estimated from the minimum emetic dose in pigeons.

Conditions affecting the efficiency of the probable therapeutic dosage of digitalis in pathological conditions in circulation are discussed. Such dosage ascertained with pigeons and given in several divided doses orally, gave complete therapeutic responses in three out of four patients. Thus, the evidence taken together indicates that the pigeon-emesis method of estimating the potency of digitalis appears to predict the probable therapeutic dose for man.

Burwell, C. Sidney, and Smith, W. Carter: The Output of the Heart in Patients with Abnormal Blood Pressures. J. of Clin. Invest. **7**: 1, 1929.

In two groups of cases one with systolic blood pressure of over 175 mm. of mercury and one with systolic blood pressure of less than 95 mm. of mercury the total cardiac output per minute per kg. of body weight and the cardiac output per 100 c.c. of oxygen absorbed did not show significant changes.

The cardiac output of all the subjects in both groups falls within the limit seen in normal healthy people. When the blood pressure is within the usual zone the averages of the cardiac output in the two groups are almost identical. The absence of variation is striking when it is observed that the average pulse pressure in the hypertensive group is 85 mm. as against 26 in the hypotensive group.

The basal metabolic rate is on the whole somewhat higher in the group with high pressures than in the group with low. The pulse rates in both groups with the exception of those of the two normal men are slightly above the low level usually attained under satisfactory basal conditions and the average rate is higher in the hypertensive just as is the metabolic rate.

These observations demonstrate that under conditions of bodily rest patients with arterial hypertension have no significant increase in the cardiac output.

Esler, James W., and White, Paul D.: Clinical Significance of Premature Beats. Arch. Int. Med. **43**: 606, 1929.

The present study consists of a series of 200 patients, 100 of whom showed premature beats and 100 normal rhythm. None of them evidenced a marked degree of auriculo-ventricular or intraventricular block. They were seen between

the years 1915 and 1926, have been studied by electrocardiograms and have been followed to the present time. The clinical diagnoses in the cases of the two groups were similar.

Premature beats which occurred at the more rapid rates in this series did not bear a more serious prognosis than those at slower rates, when allowance was made for the increase in mortality due to increased rate alone. The presence of premature beats in the series reported here added no gravity to the prognosis. The death rate was actually slightly greater in the 100 cases with normal rhythm.

Auricular premature beats and multifocal ventricular premature beats did not appear to bear a much more serious prognosis than the usual unifocal ventricular premature beat.

The authors conclude that the frequency with which premature beats occur in a given case seem to bear little relation to prognosis.

Stewart, Harold J.: A Study of Certain Effects Occasioned in Dogs by Diphtheria Toxin. Arch. Path. **7**: 767, 1929.

Following the intravenous injection into dogs of diphtheria toxin it was noted that most of these dogs showed progressive decrease in the amplitude of the R_2 and R_3 waves of the electrocardiogram. The present paper analyzes these changes in the apparent size of the heart. The analysis of the factors involved in this alteration indicates that it is due to loss of weight by the heart, although other factors possibly play a part. The author has studied the change in body weight, the number of red blood cells and the amount of hemoglobin. There was also no consistent change in the total blood volume. Histological study of the muscles of the heart did not reveal an actual destruction of the cells to account for the decrease in weight.

Otto, Harold L.: The Ventricular Electrocardiogram. Arch. Int. Med. **43**: 335, 1929.

The author has studied the nature of disturbances in the component portions of the ventricular electrocardiogram by using various preparations that would either destroy or irritate the heart muscle. In 48 experiments on dogs the heart muscle was destroyed by injections of 95 per cent solution of alcohol. Various regions of the heart were injected.

Extensive destruction of the heart muscle can be made in this way before it causes circulatory failure. The injection of an irritant like hypertonic saline solution does not significantly alter the electrocardiogram. The electrocardiographic changes which occur from injections of alcohol are due to the destruction of the muscle, irritation of the muscle playing no part.

The author has also noted that mechanical irritation of the ventricular muscle was without effect on the electrocardiogram and also that the amount of injection which was usually necessary to affect the T wave permanently was considerably less than that required to affect the QRS. Contrasted to the T wave, this portion of the electrocardiogram was stable and did not give indication of the changes which had taken place within the myocardium.

Weiss, Soma and Blumgart, Herrmann L.: The Effect of the Digitalis Bodies on the Velocity of Blood Flow Through the Lungs and on Other Aspects of the Circulation. A Study of Normal Subjects and Patients with Cardio-Vascular Disease. Jour. Clin. Invest. **7**: 11, 1929.

Strophanthin and tincture of digitalis were administered intravenously and by mouth respectively to eight normal persons. Their effect on the velocity of pul-

monary and peripheral venous blood flow, on the vital capacities of the lungs and arterial and venous pressures was observed. Amounts of these drugs corresponding to large therapeutic doses failed to change appreciably the velocity of the pulmonary blood flow and the above-mentioned aspects of the circulation in the normal subjects.

When strophanthin or tincture of digitalis in large therapeutic doses was administered to 14 patients suffering from cardiovascular disease, the velocity of the pulmonary blood flow became increased in seven, was unaltered in four, while in three patients it was definitely decreased.

Although the average pulse rate in seven patients showed a reduction of 14 beats per minute, the pulmonary circulation time showed an average reduction of 6.9 seconds which corresponds to an increase of 30 per cent in the velocity of pulmonary blood flow.

The velocity of blood flow in the pulmonary circuit is decreased in patients with circulatory failure. With clinical signs of improvement due to the administration of digitalis or to rest the velocity of this blood flow increases although the degree of the patient's improvement and the change in velocity may not be parallel.

Wolff, Louis and White, Paul D.: Auricular Fibrillation. Results of Seven Years Experience with Quinidine Sulphate Therapy. Arch. Int. Med. 43: 653, 1929.

In 1923 Viko, Marvin and White reported 71 cases of nonparoxysmal auricular fibrillation and 4 cases of auricular flutter. In 68 per cent of these patients the rhythm was restored to normal by quinidine but in only 34 per cent was it maintained during the period of observation, which varied from a few days to more than 10 months. The data obtained from the follow-up study of these patients is presented in this present article.

The second group consists of patients seen since the first report was made and therefore is composed of new patients. The total number of 70 cases comprises 62 of fibrillation and 8 of flutter. Of this entire group circus movement was abolished in 36 or 65.7 per cent.

In apparently normal hearts consisting of 7 cases in this series, premature auricular fibrillation was terminated by quinidine in 100 per cent of the cases, irrespective of the age of the patient and the duration of the fibrillation. These patients are the most satisfactory to treat. The next most responsive group is that of patients with rheumatic heart disease who are less than 41 years of age. In the hyperthyroid group the response is somewhat better than in the group of patients with hypertensive and arteriosclerotic heart disease.

When not dealing with normal hearts the most important single factor which influences the outcome of the treatment is the duration of fibrillation. This is true in a limited sense only, for the response is surprisingly high when the fibrillation has lasted less than a month. Beyond this, duration apparently is of little or no importance. Age is important in the group of patients with rheumatic heart disease. The desired response occurs in a high percentage of the young patients, but occurs in a much smaller proportion of the patients more than 40 years old. Etiology has but a minor influence on the response to quinidine therapy.

Recent congestive failure reduces the probability of success from the use of quinidine. The duration of fibrillation has not accounted for the poor response in the cases with congestive failure. A past history of congestive failure, the size of the heart when enlarged, the type of fibrillation and sex appears to be of no influence on the outcome of treatment.

Factors contributing to failure in some of the cases in this series were insufficient quinidine doses, intercurrent infections and possibly alcoholism. In this

new group of 70 patients there was one death which might possibly be attributed to quinidine but probably was not due to it. The history of fibrillation for a great many years in the absence of valvular disease and congestive failure, recent or present, is not a contraindication for quinidine therapy.

It seems highly desirable to digitalize all patients as a matter of routine before starting quinidine. Full therapeutic doses should be used. There is clinical, experimental and theoretical justification for this view. Digitalization is not indispensable in many cases but in some it will spell the difference between failure and success. Often normal rhythm may be attained with smaller doses of quinidine if digitalization has been resorted to. It may add to the comfort of the patient, improve his condition and possibly prevent fixed flutter. No harm has been observed from the combined use of digitalis and quinidine.

Quinidine is of value in preventing and terminating paroxysmal auricular fibrillation and is effective in some cases of paroxysmal tachycardia and premature beats. In cases of auricular flutter digitalis is probably more effective than quinidine. Digitalis appears to be more effective than quinidine in occasional cases of paroxysmal auricular fibrillation and paroxysmal tachycardia. In judging the value of quinidine in premature auricular fibrillation the criterion of greatest importance is the permanence of the results obtained. These follow-up studies have indicated that restored normal rhythm is permanent in a significant number of patients and although there is no definite evidence that normal rhythm prolongs life or reduces mortality, it is clearly evident that it promotes the health of the patient.

Harris, Kenneth E.: A Series of Cases of Auricular Fibrillation Treated with Quinidine Sulphate with Special Reference to the Duration of the Restored Normal Mechanism. Heart, **14**: 283, 1929.

Forty-three consecutive cases of auricular fibrillation were treated with quinidine sulphate during the period of 1921 and 1923. The immediate results, together with the after histories of those patients in whom normal rhythm was restored are now recorded. In 26 of the 43 cases (60.5 per cent) normal rhythm was restored. The 26 patients who reacted successfully have been kept under close observation for the purpose of ascertaining how long the heart rhythm would remain normal. At the end of the first month auricular fibrillation had reappeared in 9 cases, while in 17 normal rhythm persisted. By the end of 6 months fibrillation had reappeared in 2 more cases. At the end of one year fibrillation had reappeared in 16 of the original series. During the next year three more reverted so that at the end of two years 6 cases were known still to present normal rhythm. Of these 6 patients 4 resumed the condition of fibrillation after periods over two, three and one-fourth, four and one-half and seven years respectively. One has not been heard of since July, 1926, the other is still normal for four years. The two patients that have been untraced, presented normal rhythms for 317 and 1673 days after quinidine therapy.

Wolff, Louis and White, Paul D.: Auricular Standstill During Quinidine Sulphate Therapy. Heart, **14**: 294, 1929.

The two cases reported in the present communication furnish evidence that temporary auricular standstill may occur when auricular fibrillation ceases under the influence of quinidine. The effect of quinidine in this connection may be due to its poisonous action to the auricular muscle. There is experimental evidence that quinidine depresses the sino-auricular node and that it may induce intra-auricular block and auricular standstill.

Levine, Samuel A. and Fulton, Marshall N.: The Effect of Quinidine Sulphate on Ventricular Tachycardia. J. A. M. A. **92:** 1163, 1929.

Clinical experiments in ten cases showing paroxysmal or persistant tachycardia of ventricular origin indicates that quinidine sulphate has in most instances a specific effect on restoring a normal rhythm.

Ventricular tachycardia occurs occasionally in patients who have no organic heart disease but more commonly in those with coronary thrombosis. Although quinidine does not have any effect on the other complications of coronary thrombosis such as rupture of the heart or production of emboli, its beneficial influence on ventricular tachycardia is most dramatic and may be life saving.

It is highly probable that ventricular tachycardia is of the nature of a circus movement like that of auricular flutter and auricular fibrillation and that the effect of quinidine is similar in all these conditions.

Moore, Henry: Paroxysmal Ventricular Tachycardia. Irish J. Med. Sci., 754, Dec., 1928.

A case of paroxysmal tachycardia in a boy 12 years old, probably arising in the ventricular muscle is described. The patient has been under observation for more than 56 months. The attacks have become less frequent and of shorter duration. Electrocardiograms are presented showing the character of the waves during the attacks and intervals of regular sinus rhythm. The attacks occurred spontaneously, were readily induced by the administration of atropine and whether spontaneous or induced by atropine were readily terminated by giving quinidine orally. They usually started with an abrupt change in the form of the QRS complex and approximately a normal heart rate. The ventricular rate during the attack rose to about 170 per minute. The T wave in the slow atropine paroxysm was upright whenever recorded, whereas it was inverted in the slow spontaneous attacks.

Coombs, Carey F.: The Distal Phenomena that Accompany High Arterial Tension. Bristol Medico-Chirurgical J. **46:** 35, 1929.

In this address the author described the effects to be noted in the body as a result of high arterial tension. He mentions the effect in the cerebral circulation and the brain, in the peripheral muscles and other tissues. He believes that all of these phenomena can be ascribed at least in part to gradual wearing down of the elasticity of the arterial tree. He believes that the importance of obstruction in the small vessels is not substantiated by examination of the tissues.

Hare, D. C. and Karn, M. Noel: An Investigation of Blood Pressure, Pulse Rate and the Response to Exercise During Normal Pregnancy, and Some Observations after Confinement. Quart. J. Med. **22:** 381, 1929.

The object of this investigation has been to study the physiological reactions of the circulation during the course of normal pregnancy. The methods employed were blood pressure and pulse rate measurements and the response of the pulse rate to an exercise test. One hundred and six individuals are included in the study, three-fourths of whom were seen several times at intervals of four weeks or more. A suitable group of nonpregnant women were examined as controls using the same methods under the same conditions.

It was found that the average systolic blood pressure of healthy women during pregnancy is lower than the average of nonpregnant women; also the average deviation during pregnancy is less and the range is consequently slightly smaller.

Changes during the course of pregnancy show a tendency to a lower pressure in the middle period than in the earlier weeks and there is a slight but significant rise in the last three months. Any considerable rise is to be associated with the onset of a toxic condition. The mean diastolic pressure during pregnancy is not significantly different from that of nonpregnant women. During the first six months the mean pressure is below the general mean and there is a steady rise from the seventh month to a maximum in the last month which is higher than the mean for nonpregnant women. The pulse pressure is lower than that of nonpregnant women and falls with the advance of pregnancy.

Pulse rate during pregnancy is not significantly altered from the normal. The difference between the sitting and standing rates is within the range of the normal increase. The pulse rates show no significant correlation with the period of pregnancy.

An exercise test is well performed and the pulse rates after exercise are not significantly different from those of controls. In the last months of pregnancy the mean rates after exercise are below those of the preceding periods. The rates after exercise are highly correlated with the resting rate.

There is no evidence to be found in this work of embarrassment of circulation during the later months of pregnancy.

Harris, Kenneth E.: Notes on a Case of Complete Heart Block of Unusually Long Duration. Heart, **14**: 289, 1929.

Complete heart block in a healthy and active man with case notes over the remarkably long period of 28 years is here recorded. The earliest notes are from the hospital records in 1900 and the first graphic records are those taken in 1909. The patient now 50 years of age, is still vigorous and in no way incapacitated.

The first manifestations of heart block were the short signs of serious syncopal attacks. The case is unusual not only for its duration but especially because the man has enjoyed vigorous health without limitation of his capacity for physical work throughout the whole period named.

Redisch, W., and Rosler, H.: Contributions to the Knowledge of Congenital Heart Lesions. V. Capillary Studies. Wien. Arch. f. inner. Med. **16**: Part 2/3, 463, 1929.

In 36 cases of congenital heart disease, four of which have been controlled by autopsy and in 10 cases of acquired heart disease the picture of the capillaries has been studied. In morbus caeruleus there is an extreme capillary hyperemia with special involvement of the various parts of the capillaries, stasis and new formation of capillaries. With Pacchioni, the authors consider this congenital capillary dilatation as the chief cause of the extreme cyanosis, typical of severe congenital heart disease.

In two cases of stenosis of the isthmus of the aorta they have found numerous capillary aneurysms and small and thin capillaries of the toes in contradistinction to the well developed capillaries of the upper extremity. Cases with defect of the septum and open ductus Botalli showed a normal capillary picture. No connection was found between the clubbing and the capillary changes.

Nicholson, Gertrude and Shulman, Harold I. and Green, Dorothy L.: Congenital Heart Block with Report of a Case. Am. J. Dis. Child. **37**: 280, 1929.

An instance of congenital cardiac defect with peculiarities of pulse rate and rhythm is presented. The electrocardiogram shows the arrhythmia to be due to

a defect in cardiac mechanism which varies in its action. In this type of lesion of the heart, high grades of heart block are seen frequently to alternate with complete dissociation. The theory that this change is due to variance in tissue tension around the defective conducting fibers is suggested.

Aalsmeer, W. C. and Wenckebach, K. F.: The Heart and Circulatory System in Beri-Beri. Monograph, Urban and Schwarzenberg, 1929.

Beri-beri not only produces degeneration of the nerves and hydrops but is responsible for important cardiac symptoms. These so far have been explained by degeneration of the vagus nerve. Aalsmeer who studied the diseases in Java describes three forms. (1) A mild form occurring in ambulatory patients. Dyspnea and palpitation may be present in these cases and on examination the precordial pulsation is wave-like, the heart sounds are very loud and although no change in the heart size is usually made out on examination, the fluoroscope will reveal an increase in the size of the right heart. Rest and administration of vitamine B offers an effective therapy. (2) A moderately severe type. This occurs in the patients who already show edema and polyneuritis although cardiac symptoms may be absent in such cases, most of the patients complain of a feeling of pressure in the heart region, relieved on lying down. Cough, dyspnea and cyanosis are not usually present. Again the waving pulsation in the precordium is present, the heart is enlarged to right and left and a systolic murmur can be heard over the left heart. Hydrothorax may be present and is usually a part of the general edema rather than of cardiac origin. The spleen and liver are enlarged and tender. (3) An acute pernicious form of beri-beri. The chief symptoms are precordial distress localized to the sternum (Shôshin) accompanied by extreme dyspnea. The physical findings are as in the previous type excepting that the right heart is relatively much increased in size. No edema of the lungs is present, the onset is sudden and the course fatal. Intra-cardiac adrenalin is occasionally of benefit. Venesection is useful and relieves the feeling of oppression and precordial pain.

A chronic form of cardiac beri-beri has been described. This probably occurs in patients who have had the acute form of the disease and who have reverted to their deficient diet.

The blood pressure in beri-beri shows no change. The roentgenogram shows right-sided enlargement of the heart; signs of congestion of the lungs are rarely visible. The electrocardiogram shows a shortening of the conduction time with tachycardia. The P-R interval may be 0.12 second or shorter. Pathologically both right and left ventricles are dilated with increase in the size of the muscle especially on the right side. The heart muscle itself seems unchanged.

The precordium usually contains between 10 and 200 c.c. of fluid. Lung congestion is not usually present but emphysema may be found. The treatment consists of rest in bed, corrected diet and venesection. Strychnin may be used, digitalis and strophanthin are without effect. The heart symptoms are due to failure of the right heart, but it is improbable that emphysema of the lungs, changes in the pulmonary artery or degeneration of the vagus nerve could be responsible for this condition. Wenckebach believes that when the whole heart becomes weaker the right heart will fail first and this failure will be the cause of death. This probably occurs in other forms of heart disease but not in such a clearly cut manner as in beri-beri, since other types of heart disease are usually accompanied by valvular defects, fibrillation, etc. It has been shown that in the frog heart swelling of the muscle will produce some failure of contraction although the stimulus will be conducted normally, thus a similar phenomenon in beri-beri would account for the decreased cardiac activity with the more rapid conduction

time. The vitamine deficiency may act by changing the colloidal water binding capacity in certain predisposed tissues. Reversibility of this process would support this theory. Administration of the B vitamine has the same specific effect in beri-beri as thyroid has in myxedema.

Kurtz, Chester M. and White, Paul D.: The Treatment of Subacute Bacterial Endocarditis by Transfusion from Immunized Donors. New Eng. J. Med. 200: 479, 1929.

In a slowly progressing case of subacute bacterial endocarditis, immunized transfusions from donors vaccinated with a killed culture obtained from the patient's blood were tried. One massive transfusion of 1800 c.c. and five smaller ones (500 c.c. each) were given without any appreciable effect on the course of the disease which terminated fatally seventeen months after the onset. Serological studies showed the antibody titer to be higher in the patient than in any of the donors. The authors believe that this case indicates that patients with this infection have an opportunity to develop a certain amount of active immunity because the Streptococcus viridans is of rather low virulence and the disease progresses slowly. It is probable that the immunity is greater than can be induced by vaccinating a healthy donor.

Book Reviews

CLINICAL ELECTROCARDIOGRAMS, THEIR INTERPRETATION AND SIGNIFICANCE. By Fredrick A. Willius, M.D. Section on Cardiology, The Mayo Clinic, Rochester, Minnesota, and Associate Professor of Medicine, The Mayo Foundation, University of Minnesota. W. B. Saunders Company, 1929, Philadelphia, pp. 219.

This volume, one of the Mayo Clinic monographs, is, as its title indicates, a clinical guide to the reading and interpretation of electrocardiograms. The book is carefully planned, omitting all discussion of method, technic and theory, but considering in order the normal electrocardiogram and the various deviations from this: ventricular preponderance, the arrhythmias, individual wave changes, dextrocardia, coronary thrombosis, and records obtained from the dying heart. The text is clear and concise, written in condensed direct style, and valuable because of the author's wide experience. The chief value of the book, however, lies in its illustrations. The 368 figures have been selected with care to show not only typical tracings but also transitional changes and combinations of several abnormalities. The figures are clear cut and are accompanied by unusually full legends. The tracings and legends comprise a fairly complete text and reference book, but for those who wish to pursue more detailed study there is a good bibliography with references arranged at the end of each chapter. An adequate index enhances the value of the text. This book should be of value to all who are interested in the interpretation and significance of electrocardiograms.

DISEASES OF THE HEART AND VESSELS. By Ernst Edens. With 239 partially colored pictures. 1057 pages. Berlin. Julius Springer, 1929.

As the author says in the introduction, this book intends to give a critical review of our present knowledge of the diseases of the heart and vessels and the appropriate therapy. After an abstract of the historical development, the anatomy and physiology of the circulatory system are given. The methods for the examination of the circulatory system are described. Following this then is a study of the valvular diseases with their consequences and cardiac insufficiency. A special chapter is devoted to the functional test of the heart and the vessels. A great space is occupied by the therapy of cardiac insufficiency which covers all the problems of modern treatment of heart patients. The physical methods of treatment are given the consideration which they deserve. The next chapter contains the description of valvular lesions with their clinical and therapeutic peculiarities. Next follow the malformations of the heart and the diseases of the heart muscle. The mutual relationship between the heart and factors which make up body constitution is discussed. A special chapter is devoted to the study of mechanical conditions under which the heart is working and its changes under pathological conditions. A thorough chapter on the irregular activity of the heart and its treatment closes the part of the book dealing with the heart alone. A chapter follows on the diseases of the pericardium.

The diseases of the vessels are separated in three divisions: those of the arteries, the veins and the capillaries. An especially broad discussion on angina pectoris and a short review of the neurosis of the heart and vessels finish this part of the book. The text is accompanied by excellent pictures, curves, tables and electrocardiograms. The print is good. An index with the authors' names and the subjects and an extremely comprehensive accumulation of the literature (246 pages) complete the book and make it a very valuable addition to the well-known textbooks of heart disease for the student, the practitioner and the research worker.